~~10/513699~~ 10/561,101

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| | | | |
|---|---|---|---|
| NEWS | 1 | | Web Page for STN Seminar Schedule - N. America |
| NEWS | 2 | JUL 02 | LMEDLINE coverage updated |
| NEWS | 3 | JUL 02 | SCISEARCH enhanced with complete author names |
| NEWS | 4 | JUL 02 | CHEMCATS accession numbers revised |
| NEWS | 5 | JUL 02 | CA/CAplus enhanced with utility model patents from China |
| NEWS | 6 | JUL 16 | CAplus enhanced with French and German abstracts |
| NEWS | 7 | JUL 18 | CA/CAplus patent coverage enhanced |
| NEWS | 8 | JUL 26 | USPATFULL/USPAT2 enhanced with IPC reclassification |
| NEWS | 9 | JUL 30 | USGENE now available on STN |
| NEWS | 10 | AUG 06 | CAS REGISTRY enhanced with new experimental property tags |
| NEWS | 11 | AUG 06 | BEILSTEIN updated with new compounds |
| NEWS | 12 | AUG 06 | FSTA enhanced with new thesaurus edition |
| NEWS | 13 | AUG 13 | CA/CAplus enhanced with additional kind codes for granted patents |
| NEWS | 14 | AUG 20 | CA/CAplus enhanced with CAS indexing in pre-1907 records |
| NEWS | 15 | AUG 27 | Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB |
| NEWS | 16 | AUG 27 | USPATOLD now available on STN |
| NEWS | 17 | AUG 28 | CAS REGISTRY enhanced with additional experimental spectral property data |
| NEWS | 18 | SEP 07 | STN AnaVist, Version 2.0, now available with Derwent World Patents Index |
| NEWS | 19 | SEP 13 | FORIS renamed to SOFIS |
| NEWS | 20 | SEP 13 | INPADOCDB enhanced with monthly SDI frequency |
| NEWS | 21 | SEP 17 | CA/CAplus enhanced with printed CA page images from 1967-1998 |
| NEWS | 22 | SEP 17 | CAplus coverage extended to include traditional medicine patents |

NEWS EXPRESS 05 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 05 SEPTEMBER 2007.

| | |
|---|---|
| NEWS HOURS | STN Operating Hours Plus Help Desk Availability |
| NEWS LOGIN | Welcome Banner and News Items |
| NEWS IPC8 | For general information regarding STN implementation of IPC 8 |

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10/513699

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:47:08 ON 18 SEP 2007

=> file reg

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 15:47:13 ON 18 SEP 2007
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STRUCTURE FILE UPDATES: 17 SEP 2007 HIGHEST RN 947369-26-8
DICTIONARY FILE UPDATES: 17 SEP 2007 HIGHEST RN 947369-26-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10561101claim79.str

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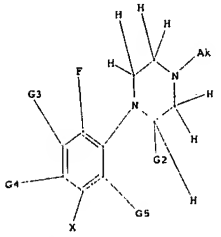
=> d l1
L1 HAS NO ANSWERS
L1 STR

<12/04/2007> Erich Leese

10/513699



G1 C,H,Ak

G2 X,Ak,CF2,CF3

G3 X,CN

G4 C,O,Ak,CF3,X

G5 X,Me,CH2,CH,Et

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
FULL SEARCH INITIATED 15:48:01 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 8971 TO ITERATE

100.0% PROCESSED 8971 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L2 0 SEA SSS FUL L1

=> file reg

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 182.00 | 182.21 |

FILE 'REGISTRY' ENTERED AT 16:01:11 ON 18 SEP 2007
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DICTIONARY FILE UPDATES: 17 SEP 2007 HIGHEST RN 947369-26-8

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

<12/04/2007> Erich Leese

10/513699

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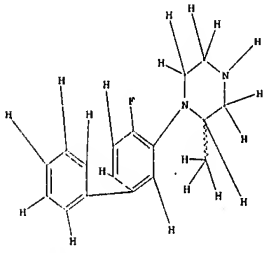
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10561101stereounspecific.str

L3 STRUCTURE UPLOADED

=> d l3
L3 HAS NO ANSWERS
L3 STR



G1 C,H,Ak

G2 X,Ak,CF2,CF3

G3 X,CN

G4 C,O,Ak,CF3,X

G5 X,Me,CH2,CH,Et

Structure attributes must be viewed using STN Express query preparation.

=> s l3 full
FULL SEARCH INITIATED 16:01:40 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 416 TO ITERATE

100.0% PROCESSED 416 ITERATIONS 4 ANSWERS
SEARCH TIME: 00.00.01

<12/04/2007> Erich Leese

L4 4 SEA SSS FUL L3

=> file caplus
COST IN U.S. DOLLARS — SINCE FILE ENTRY: 172.10 — TOTAL SESSION: 354.31

FILE 'CAPLUS' ENTERED AT 16:01:46 ON 18 SEP 2007
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FILE COVERS 1907 - 18 Sep 2007 VOL 147 ISS 13
FILE LAST UPDATED: 17 Sep 2007 (20070917/ED)

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http://www.cas.org/infopolicy.html

=> s l4 full
L5 1 L4

=> d ibib abs hitstr

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:158653 CAPLUS
DOCUMENT NUMBER: 142:261560
TITLE: Preparation of N-phenyl-piperazine derivatives and methods of prophylaxis or treatment of 5-HT2C receptor associated diseases
INVENTOR(S): Smith, Brian; Tsai, James; Chen, Rita
PATENT ASSIGNEE(S): Arena Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005016902 | A1 | 20050224 | WO 2004-US19540 | 20040617 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

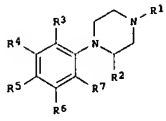




TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| AU 2004265243 | A1 | 20050224 | AU 2004-265243 | 20040617 |
| CA 2529750 | A1 | 20050224 | CA 2004-2529750 | 20040617 |
| EP 1644347 | A1 | 20060412 | EP 2004-776755 | 20040617 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| CN 1809545 | A | 20060726 | CN 2004-80017001 | 20040617 |
| BR 2004011661 | A | 20060829 | BR 2004-11661 | 20040617 |
| JP 2007523861 | T | 20070823 | JP 2006-517403 | 20040617 |
| MX 2005PA13365 | A | 20060405 | MX 2005-PA13365 | 20051208 |
| IN 2006KN00115 | A | 20070622 | IN 2006-KN115 | 20060113 |
| US 2007179155 | A1 | 20070802 | US 2006-561101 | 20060526 |
| PRIORITY APPLN. INFO.: | | | US 2003-480045P | P 20030620 |
| | | | WO 2004-US19540 | W 20040617 |

OTHER SOURCE(S): CASREACT 142:261560; MARPAT 142:261560
GI



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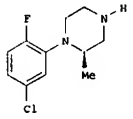


II

AB Title compds. I (wherein R1 = H, alkyl; R2 = alk(en)yl, haloalkyl; R3, R4, R5, R6, R7 = independently H, acyl, acyloxy, acylthioxy, alk(en)yl, halo/carbo/alkoxy, alkylcarboxamido, halo, OH, SH, Ph, halo/alkylsulfinyl, alkylsulfonamido, halo/alkylsulfonyl, halo/alkylthio, NH2, di/alkylamino, CN, haloalkyl; and their pharmaceutically acceptable salts, solvates or hydrates; with the proviso that certain compds. are excluded) were prepared as 5-HT2C receptor modulators, in particular agonists. Thus, II•xHCl was prepared by Pd-coupling of 2-Bromo-4-chloro-1-fluorobenzene with



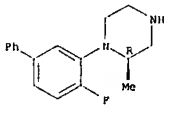


4-(tert-butoxycarbonyl)-(R)-2-methylpiperazine. Intracellular IP3 accumulation assay (EC50 = 8.0 nM against the 5-HT2C receptor) and inhibition of food intake in food-deprived rats (see chart) were used to test the bioactivity of II. Certain compds. are selective for the 5-HT2C receptor compared to the 5-HT2A and 5-HT2B receptors; for example II has an EC50 value of 529 nM against the 5-HT2A receptor and is essentially inactive against the -5HT2B receptor. I are useful for the prophylaxis or treatment of 5-HT2c receptor associated diseases or disorders, such as, obesity, Alzheimer Disease, erectile dysfunction and related disorders.

IT 845741-28-8P, (R)-1-(4-Fluorobiphenyl-3-yl)-2-methylpiperazine hydrochloride 845741-29-9P, (S)-1-(4-Fluorobiphenyl-3-yl)-2-methylpiperazine hydrochloride 845742-44-1P, (R)-1-(4-Fluorobiphenyl-3-yl)-2-methylpiperazine 845742-45-2P, (S)-1-(4-Fluorobiphenyl-3-yl)-2-methylpiperazine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of N-phenylpiperazines as 5-HTC receptor modulators)

RN 845741-28-8 CAPLUS
CN Piperazine, 1-(4-fluoro[1,1'-biphenyl]-3-yl)-2-methyl-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

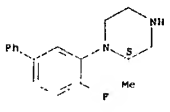
Absolute stereochemistry.



•x HCl

RN 845741-29-9 CAPLUS
CN Piperazine, 1-(4-fluoro[1,1'-biphenyl]-3-yl)-2-methyl-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



•x HCl





RN 845742-44-1 CAPLUS
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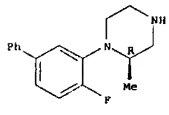
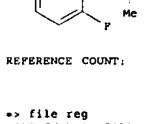
Absolute stereochemistry.



RN 845742-45-2 CAPLUS
CN Piperazine, 1-(4-fluoro[1,1'-biphenyl]-3-yl)-2-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) — SINCE FILE ENTRY: -0.78 — TOTAL SESSION: -0.78
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DICTIONARY FILE UPDATES: 17 SEP 2007 HIGHEST RN 947369-26-8

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http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10561101final.str

L6 STRUCTURE UPLOADED

=> d l6
L6 HAS NO ANSWERS
L6 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l6 full
FULL SEARCH INITIATED 16:08:30 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 602595 TO ITERATE

100.0% PROCESSED 602595 ITERATIONS 1347 ANSWERS
SEARCH TIME: 00.00.05

L7 1347 SEA SSS FUL L6

=> file caplus
COST IN U.S. DOLLARS

| | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 172.10 | 536.38 |

| DISCOUNT AMOUNTS (QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | 0.00 | -0.78 |

FILE 'CAPLUS' ENTERED AT 16:08:40 ON 18 SEP 2007
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FILE COVERS 1907 - 18 Sep 2007 VOL 147 ISS 13
FILE LAST UPDATED: 17 Sep 2007 (20070917/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l7 full
L8 201 L7

=> s l8 and py<2003
22890048 PY<2003
L9 134 L8 AND PY<2003

=> d ibib abs hitstr tot

L9 ANSWER 1 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:284138 CAPLUS
DOCUMENT NUMBER: 142:355256
TITLE: Preparation of tricyclic-substituted piperidinols and analogs as chemokine receptor antagonists
INVENTOR(S): Luly, Jay R.; Nakasato, Yoshisuke; Ohshima, Etsuo; Harriman, Geraldine C. B.; Carson, Kenneth G.; Ghosh, Shomir; Elder, Amy M.; Mattia, Karen M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 194 pp., Cont.-in-part of U.S. Ser. No. 989,086, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2005070549 | A1 | 20050331 | US 2004-487168 | 20041007 |
| US 7186729 | B2 | 20070306 | | |
| US 6613905 | B1 | 20030902 | US 1998-148823 | 19980904 |
| US 6329385 | B1 | 20011211 | US 1999-235102 | 19990121 <-- |
| US 2002119973 | A1 | 20020829 | US 1999-362837 | 19990728 <-- |
| US 6509346 | B2 | 20030121 | | |
| US 2002169155 | A1 | 20021114 | US 2001-989086 | 20011121 <-- |
| WO 2003045942 | A2 | 20030605 | WO 2002-US36953 | 20021113 |
| WO 2003045942 | A3 | 20030912 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2007060592 | A1 | 20070315 | US 2006-595653 | 20061110 |
| AU 2007200261 | A1 | 20070208 | AU 2007-200261 | 20070123 |

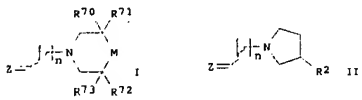
| PRIORITY APPLN. INFO.: | | |
|---|---|---|
| US 1998-148823 | A2 | 19980904 |
| US 1999-235102 | A2 | 19990121 |

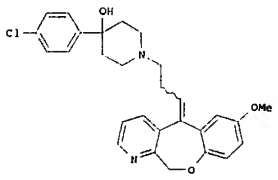




| | | |
|---|---|---|
| US 1999-362837 | A2 | 19990728 |
| US 2000-627886 | B2 | 20000728 |
| US 2001-989086 | B2 | 20011121 |
| WO 2002-US36953 | W | 20021113 |
| US 1998-10320 | B2 | 19980121 |
| AU 2002-352772 | A3 | 20021113 |
| US 2004-487168 | A1 | 20041007 |

OTHER SOURCE(S): MARPAT 142:355256
GI




AB Therapeutically effective compds. I [Z = (un)substituted heterocyclic ring fused to one or more carbocyclic aromatic rings; n = 1-4; M = NR2, CR1R2; R1 = H, OH, N3, etc.; R2 = OH, halo, acyl, aryl, etc.; R70, R71 = H, OH, N3, etc.; R72, R73 = O, N2, halo, etc.] and II [Z, n are defined as above; R2 = OH, halo, acyl, aryl, etc.] were prepared for treatment of diseases associated with aberrant leukocyte recruitment and/or activation (no data). I and II displayed chemokine binding activities with IC50 values ranging from < 1 μM to < 1000 μM. Thus, the [(1]benzoxepino[2,3-b]pyridinylidene)propyl]piperidinol III was prepared in three steps by reaction of 5,11-dihydro-7-methoxy[1]benzoxepino[2,3-b]pyridin-5-one with cyclopropylmagnesium bromide in THF, followed by ring cleavage-dehydration-bromination with HBr, and addition of 4-(4-chlorophenyl)-4-hydroxypiperidine to the bromide in DMF. Major and minor isomers were separated The pharmaceutical compns. comprising the compound I or II is disclosed.

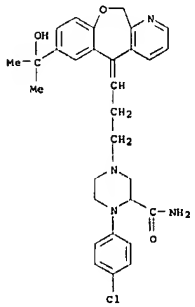
IT 849105-73-3P 849105-74-4P 849105-75-5P
849105-85-7P 849105-86-8P 849105-87-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tricyclic piperidinols and pyrrolidines as chemokine receptor antagonists for treatment of diseases associated with aberrant leukocyte recruitment and activation)

RN 849105-73-3 CAPLUS

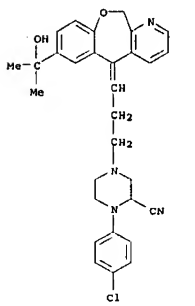




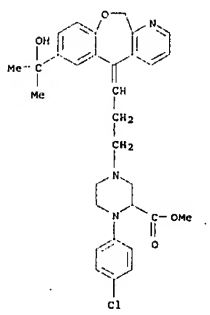
CN 2-Piperazinecarboxamide, 1-(4-chlorophenyl)-4-[3-[7-(1-hydroxy-1-methylethyl)[1]benzoxepino[3,4-b]pyridin-5(11H)-ylidene]propyl]- (9CI) (CA INDEX NAME)




RN 849105-74-4 CAPLUS
CN 2-Piperazinecarbonitrile, 1-(4-chlorophenyl)-4-[3-[7-(1-hydroxy-1-methylethyl)[1]benzoxepino[3,4-b]pyridin-5(11H)-ylidene]propyl]- (9CI) (CA INDEX NAME)

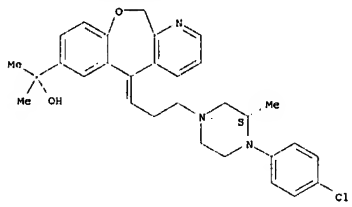


RN 849105-75-5 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-(4-chlorophenyl)-4-[3-[7-(1-hydroxy-1-methylethyl)[1]benzoxepino[3,4-b]pyridin-5(11H)-ylidene]propyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 849105-85-7 CAPLUS
CN [1]Benzoxepino[3,4-b]pyridine-7-methanol, 5-[3-[(3S)-4-(4-chlorophenyl)-3-methyl-1-piperazinyl]propylidene]-5,11-dihydro- α,α-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



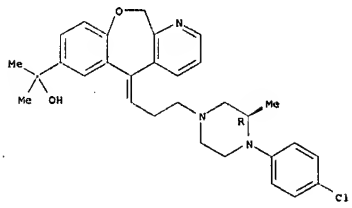
RN 849105-86-8 CAPLUS
CN [1]Benzoxepino[3,4-b]pyridine-7-methanol, 5-[3-[(3R)-4-(4-chlorophenyl)-3-methyl-1-piperazinyl]propylidene]-5,11-dihydro- α,α-dimethyl-



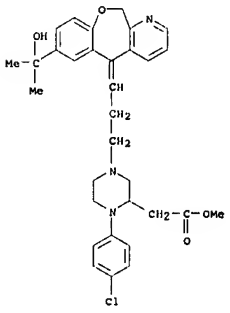


(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 849105-87-9 CAPLUS
CN 2-Piperazineacetic acid, 1-(4-chlorophenyl)-4-[3-[7-(1-hydroxy-1-methylethyl)[1]benzoxepino[3,4-b]pyridin-5(11H)-ylidene]propyl]-, methyl ester (9CI) (CA INDEX NAME)



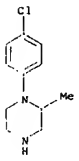
IT 55117-80-1P, 1-(4-Chlorophenyl)-2-methylpiperazine
849106-48-5P, 4-(4-Chlorophenyl)-3-methylpiperazine-1-carboxylic acid tert-butyl ester 849106-90-7P 849106-91-8P
849107-16-0P 849107-17-1P 849107-18-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)



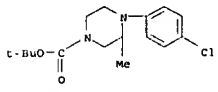


(preparation of tricyclic piperidinols and pyrrolidines as chemokine receptor antagonists for treatment of diseases associated with aberrant leukocyte recruitment and activation)

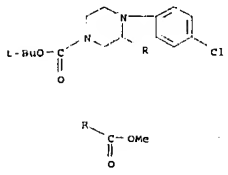
RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



RN 849106-48-5 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(4-chlorophenyl)-3-methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



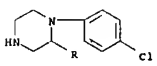
RN 849106-90-7 CAPLUS
CN 1,3-Piperazinedicarboxylic acid, 4-(4-chlorophenyl)-, 1-(1,1-dimethylethyl) 3-methyl ester (9CI) (CA INDEX NAME)



RN 849106-91-8 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-(4-chlorophenyl)-, methyl ester (9CI) (CA INDEX NAME)

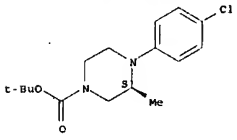






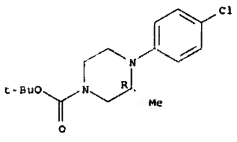
RN 849107-16-0 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(4-chlorophenyl)-3-methyl-, 1,1-dimethylethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

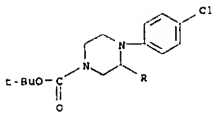


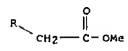
RN 849107-17-1 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(4-chlorophenyl)-3-methyl-, 1,1-dimethylethyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 849107-18-2 CAPLUS
CN 2-Piperazineacetic acid, 1-(4-chlorophenyl)-4-[(1,1-dimethylethoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)





REFERENCE COUNT: 151 THERE ARE 151 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:485162 CAPLUS
DOCUMENT NUMBER: 141:38534
TITLE: Preparation of aromatic sultone hydroxamic acid metalloprotease inhibitors
INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Boehm, Terri L.; Carroll, Jeffrey N.; Decrescenzo, Gary A.; Fobian, Yvette M.; Freskos, John N.; Getman, Daniel P.; McDonald, Joseph J.; Li, Madeleine H.; Hockerman, Susan L.; Howard, Susan C.; Kolodziej, Steve A.; Mischke, Deborah A.; Rico, Joseph G.; Stehle, Nathan W.; Tollefson, Michael B.; Vernier, William F.; Villamil, Clara I.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: U.S., 403 pp., Cont.-in-part of U.S. Ser. No. 311,837.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 6750228 | B1 | 20040615 | US 2000-570731 | 20000512 |
| US 2001014688 | A1 | 20010816 | US 1998-191129 | 19981113 <-- |
| US 2001039287 | A1 | 20011108 | US 1999-256948 | 19990224 <-- |
| CA 2372934 | A1 | 20001123 | CA 2000-2372934 | 20000515 <-- |
| WO 2000069821 | A1 | 20001123 | WO 2000-US6719 | 20000515 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1183239 | A1 | 20020306 | EP 2000-930088 | 20000515 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |





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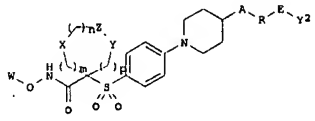
|---|---|---|---|---|
| HU 200201680 | A2 | 20020928 | HU 2002-1680 | 20000515 <-- |
| BR 2000010562 | A | 20030610 | BR 2000-10562 | 20000515 |
| JP 2003520196 | T | 20030702 | JP 2000-618238 | 20000515 |
| AU 766792 | B2 | 20031023 | AU 2000-47970 | 20000515 |
| NZ 515217 | A | 20040430 | NZ 2000-515217 | 20000515 |
| US 2002177588 | A1 | 20021128 | US 2001-954451 | 20010917 <-- |
| US 6750233 | B2 | 20040615 | | |
| ZA 2001009006 | A | 20021202 | ZA 2001-9006 | 20011031 <-- |
| NO 2001005543 | A | 20020110 | NO 2001-5543 | 20011113 <-- |
| MX 2001PA11569 | A | 20050620 | MX 2001-PA11569 | 20011113 |
| US 2003073718 | A1 | 20030417 | US 2001-989943 | 20011121 |
| US 6683093 | B2 | 20040127 | | |
| US 2004209914 | A1 | 20041021 | US 2003-730403 | 20031208 |
| US 2004235810 | A1 | 20041125 | US 2003-747796 | 20031229 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1997-66007P | P | 19971114 |
| US 1998-95347P | P | 19980804 |
| US 1998-101080P | P | 19980918 |
| US 1999-256948 | B2 | 19990224 |
| US 1999-311837 | A2 | 19990514 |
| US 1998-95601P | P | 19980806 |
| US 1998-186410 | B2 | 19981105 |
| US 1998-191129 | B2 | 19981113 |
| US 2000-570731 | A | 20000512 |
| WO 2000-US6719 | W | 20000515 |
| US 2001-989943 | A3 | 20011121 |

OTHER SOURCE(S): MARPAT 141:38534
GI



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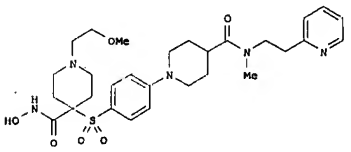


II

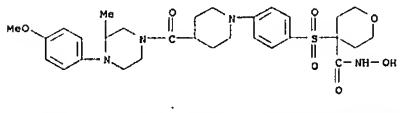
AB A treatment process is disclosed that comprises administering an effective amount of an aromatic sulfone hydroxamic acid I [W = H, cation, certain acyl or thioacyl groups; m, n, p = 0-2; (m+n+p) = 1 to 4; Z = (un)substituted NH; X, Y = (un)substituted CH2; A = bond, O, S, (un)substituted NH, COO, OCO,



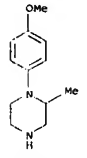


CH:CH, C.tplbond.C, N:N, NHNH, NHCOO, (un)substituted CONH, NHCO, etc.; R = alkylene, arylene, heteroarylene, etc., with provisos; E = bond, CONH, NHCO, CO, SO2, NHSO2, SO2NH, S, etc.; Y2 = absent, H, alkyl, alkoxy, aryl, aryloxy, heteroaryl, etc.] to a host having a condition associated with pathol. matrix metalloprotease (MMP) activity. I exhibit excellent inhibitory activity of one or more MMP enzymes, such as MMP-2, MMP-9 and MMP-13, while exhibiting substantially less inhibition of (at least) MMP-1 (biol. data given). Also disclosed are metalloprotease inhibitor compds. having such selective activities, processes for manufacture of such compds., and pharmaceutical compns. using such inhibitors. The compds. are potentially useful against a wide variety of conditions, notably as antiosteoarthritic, antiangiogenesis, and antitumor agents. Over 900 example compds. are listed, most with supporting phys. data, and many with synthetic details. E.g., a multi-step synthesis of the compound II.2HCl was given.

IT 308821-73-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of aromatic sultone hydroxamic acids as metalloprotease inhibitors)
RN 308821-73-0 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[4-[[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]carbonyl]-1-piperidinyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



IT 35947-12-7, 1-(4-Methoxyphenyl)-2-methylpiperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of aromatic sultone hydroxamic acids as metalloprotease inhibitors)
RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



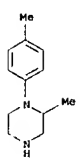
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS





RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:551964 CAPLUS
DOCUMENT NUMBER: 140:195578
TITLE: Customization of a commercially available prepare scale SFC system to provide enhanced capabilities
AUTHOR(S): Olson, Jeff; Pan, Jeff; Hochlowski, Jill; Searle, Philip; Blanchard, Dave
CORPORATE SOURCE: Abbot Laboratories, IL, USA
SOURCE: JALA (2002), 7(4), 69-74
CODEN: JALLFO; ISSN: 1535-5535
PUBLISHER: Association for Laboratory Automation
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Preparative Scale Supercrit. Fluid Chromatog. is emerging as a powerful alternative to HPLC for the purification and separation of complex chemical reaction mixts. Advantages include greatly reduced solvent usage (and thus lower cost and environmental impact), higher throughput, and in some cases higher resolution. While there are com. available prepare SFC instruments, none currently offer all the features desired by many medicinal chemists engaged in the drug discovery process. These include: the ability to collect an unlimited number of fractions per sample with high recovery and negligible carryover, fully automated capacity to collect several hundred fractions, and the ability to collect fractions into the same disposable test tubes and racks which are already employed in HPLC. This article describes the customization of a preparatory scale SFC system purchased from Berger Instruments, Inc., Newark, DE. (a subsidiary Mettler-Toledo International, Inc., of Greifensee, Switzerland) in order to provide these capabilities.
IT 35947-11-6P, 1-(4-Methylphenyl)-2-methylpiperazine
RL: ANT (Analyte); PUR (Purification or recovery); ANST (Analytical study); PREP (Preparation)
(customization of a com. available prepare scale supercrit. fluid chromatog. (SFC) system to provide enhanced capabilities)
RN 35947-11-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)- (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

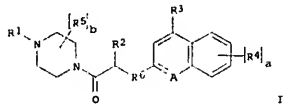
L9 ANSWER 4 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:946267 CAPLUS

DOCUMENT NUMBER: 138:24727
TITLE: Preparation of 2-[(piperazinocarbonylmethyl)aminocarbonyl]quinolines as platelet adenosine diphosphate receptor antagonists
INVENTOR(S): Bryant, Judi A.; Buckman, Brad O.; Islam, Imadul; Mohan, Raju; Morrissey, Michael M.; Wei, Guo Pin; Xu, Wei; Yuang, Shendong
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 208 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002098856 | A2 | 20021212 | WO 2002-US17821 | 20020606 <-- |
| WO 2002098856 | A3 | 20040304 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2003060474 | A1 | 20030327 | US 2002-163742 | 20020605 |
| US 6861424 | B2 | 20050301 | | |
| AU 2002316191 | A1 | 20021216 | AU 2002-316191 | 20020606 <-- |
| EP 1412349 | A2 | 20040428 | EP 2002-746471 | 20020606 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004532886 | T | 20041028 | JP 2003-501845 | 20020606 |
| US 2005038037 | A1 | 20050217 | US 2004-947579 | 20040922 |
| US 7026323 | B2 | 20060411 | | |
| US 2005065163 | A1 | 20050324 | US 2004-947635 | 20040922 |
| US 6995156 | B2 | 20060207 | | |
| US 2006135532 | A1 | 20060622 | US 2006-347768 | 20060202 |
| US 7176207 | B2 | 20070213 | | |

PRIORITY APPLN. INFO.: US 2001-296498P P 20010606
US 2002-163742 A 20020605
WO 2002-US17821 W 20020606
US 2004-947579 A3 20040922

OTHER SOURCE(S): MARPAT 138:24727
GI

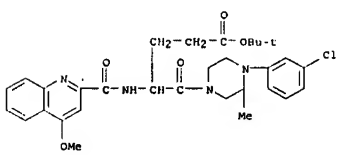


I



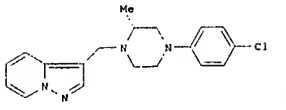


AB The title compds. [I; a, b = 1-4; A = CH, N; R1 = H, alkyl, aryl, etc.; R2 = H, alkyl, aryl, etc.; R3 = H, alkyl, OH, etc.; R4 = H, alkyl, alkoxy, etc.; R5 = H, alkyl, hydroxyalkyl, etc.; R6 = NR7CO, CONR7; R7 = H, alkyl, carboxyalkyl, alkoxycarbonylalkyl], useful as inhibitors of platelet aggregation and thrombus formation, were prepared and formulated. Thus, amidation of 7-methyl-4-hydroxy-2-carboxyquinoline with 4-ethoxycarbonyl-1-[1-amino-3-(1,1-dimethylethoxycarbonyl)propyl]carbonylpiperazine (preparation of both reactants given) afforded 68% I (R1 = CO2Et; R2 = tert-BuOCOCH2CH2; R3 = OH; R4 = 7-Me; R5 = H; R6 = NHCO; A = N). The compds. I demonstrated their ability to inhibit the binding of [33P]-2-methylthio-ADP binding to the human platelet ADP receptor and the rat platelet ADP receptor.
IT 478004-45-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-[(piperazinocarbonylmethyl)aminocarbonyl]quinolines as platelet ADP receptor antagonists)
RN 478004-45-4 CAPLUS
CN 1-Piperazinepentanoic acid, 4-(3-chlorophenyl)-γ-[[(4-methoxy-2-quinolinyl)carbonyl]amino]-3-methyl-δ-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)





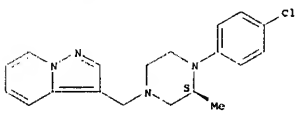




I

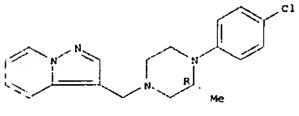
AB By employing yeast enzymes, natural amino acids and Jacobsen's catalyst as sources of chirality, pyrazolo[1,5-a]pyridine deriva. with central and planar chirality were prepared as analogs of the dopamine D4 receptor ligand FAUC 113. In vitro binding expts. displayed enhanced D2 and D3 affinity for both enantiomers of the [2.2]paracyclophane derivative The C-methylpiperazine (R)-I revealed excellent D4 selectivity.
IT 511255-13-3P 511255-27-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and activity of analogs of the dopamine D4 receptor ligand FAUC 113 with planar and central chirality)
RN 511255-13-3 CAPLUS
CN Pyrazolo[1,5-a]pyridine, 3-[[(3S)-4-(4-chlorophenyl)-3-methyl-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 511255-27-9 CAPLUS
CN Pyrazolo[1,5-a]pyridine, 3-[[(3R)-4-(4-chlorophenyl)-3-methyl-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



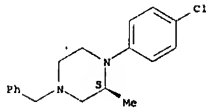
IT 511254-97-0P 511255-00-8P 511255-18-8P
511255-22-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and activity of analogs of the dopamine D4 receptor ligand FAUC





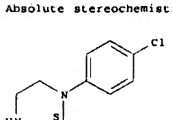
113 with planar and central chirality)
RN 511254-97-0 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



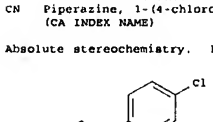
RN 511255-00-8 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



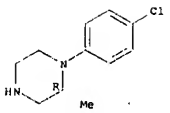
RN 511255-18-8 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl-4-(phenylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 511255-22-4 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

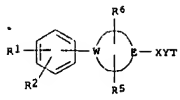
L9 ANSWER 6 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:714060 CAPLUS
DOCUMENT NUMBER: 137:232677
TITLE: Preparation of heterocyclylphenyls for treatment of thromboembolic diseases and tumors
INVENTOR(S): Mederski, Werner; Cezanne, Bertram; Dorsch, Dieter; Tsaklakidis, Christos; Gleitz, Johannes; Barnes, Christopher
PATENT ASSIGNEE(S): Merck Patent Gmbh, Germany
SOURCE: Ger. Offen., 28 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10112768 | A1 | 20020919 | DE 2001-10112768 | 20010316 <-- |
| CA 2440954 | A1 | 20020926 | CA 2002-2440954 | 20020227 <-- |
| WO 2002074765 | A1 | 20020926 | WO 2002-EP2092 | 20020227 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002249246 | A1 | 20021003 | AU 2002-249246 | 20020227 <-- |
| EP 1368341 | A1 | 20031210 | EP 2002-718165 | 20020227 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| HU 200303539 | A2 | 20040128 | HU 2003-3539 | 20020227 |
| CN 1496361 | A | 20040512 | CN 2002-806536 | 20020227 |
| JP 2004527514 | T | 20040909 | JP 2002-573774 | 20020227 |
| MX 2003PA08216 | A | 20040129 | MX 2003-PA8216 | 20030911 |
| US 2004082563 | A1 | 20040429 | US 2003-471768 | 20030916 |
| ZA 2003008028 | A | 20050117 | ZA 2003-8028 | 20031015 |

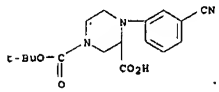
PRIORITY APPLN. INFO.: DE 2001-10112768 A 20010316
WO 2002-EP2092 W 20020227
OTHER SOURCE(S): MARPAT 137:232677
GI







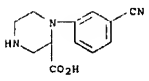
AB Title compds. [I; R1 = H, cyano, (substituted) C(:NH)NH2, CON(R3)2, [C(R4)2]nN(R3)2, etc.; R2, R5, R6 = H, halo, A, OR3, N(R3)2, NO2, cyano, [C(R4)2]nAr, [C(R4)2]nHet, [C(R4)2]ncycloalkyl, etc; R3 = H, A, [C(R4)2]nAr, [C(R4)2]nHet, [C(R4)2]ncycloalkyl; R4 = H, A; W = N, CR3; EW = 3-7 membered (substituted) (saturated) (benzo-, heterocyclyl-condensed) (hetero)cyclyl; X = [C(R4)2]nCONR3[C(R4)2]n, [C(R4)2]nNR3CO[C(R4)2]n, etc; Y = alkylene, cycloalkylene, heterocyclyldiyl, aryldiyl; T = (substituted) (bi)heterocyclyl; A = (branched) (O-, S-, CH:CH-interrupted) (fluorinated) C1-6 alkyl; Ar = (substituted) Ph, naphthyl, biphenyl; Het = (substituted) (aromatic) (bi)heterocyclyl; n = 0-2], were prepd as inhibitors of factor Xa and VIIa (no data). Thus, a mixture of 4-(tert-butoxycarbonyl)-1-(3-cyanophenyl)piperazine-2-carboxylic acid, 1-(4-aminophenyl)piperidin-2-one, N-(3-dimethylaminopropyl)-N-ethylcarbodiimide hydrochloride, and hydroxybenzotriazole hydrate in DMF was stirred with 4-methylmorpholine for 18 h at room temperature to give 4-(3-cyanophenyl)-3-[4-(2-oxopiperidin-1-yl)phenylcarbamoyl]piperazine-1-carboxylic acid tert-Bu ester which was stirred with DMSO, K2CO3, and H2O2 in MeOH for 2 h at room temperature to give (3-carbamoylphenyl)-3-[4-(2-oxopiperidin-yl)phenylcarbamoyl]piperazine-1-carboxylic acid tert-Bu ester. The latter was treated with HCl in dioxane for 1 h to give 1-[(3-carbamoylphenyl)-piperazin-2-yl]-N-[4-(2-oxopiperidin-1-yl)phenyl]amide.
IT 459132-99-1P 459133-00-7P 459133-05-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclylphenyls for treatment of thromboembolic diseases and tumors)
RN 459132-99-1 CAPLUS
CN 1,3-Piperazinedicarboxylic acid, 4-(3-cyanophenyl)-, 1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 459133-00-7 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-(3-cyanophenyl)-, monopotassium salt (9CI) (CA INDEX NAME)

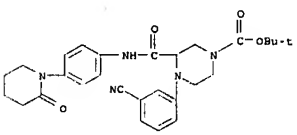






● K

RN 459133-05-2 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(3-cyanophenyl)-3-[[[4-(2-oxo-1-piperidinyl)phenyl]amino]carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



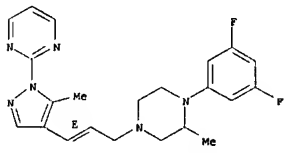
L9 ANSWER 7 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:469715 CAPLUS
DOCUMENT NUMBER: 137:384813
TITLE: Synthesis and antitumor activity of novel pyrimidinyl pyrazole derivatives. II. Optimization of the phenylpiperazine moiety of 1-[5-methyl-1-(2-pyrimidinyl)-4-pyrazolyl]-3-phenylpiperazinyl-1-trans-propenes
AUTHOR(S): Naito, Hiroyuki; Ohsuki, Satoru; Sugimori, Masamichi; Atsumi, Ryo; Minami, Megumi; Nakamura, Yoshihide; Ishii, Mineko; Hirotani, Kenji, Kumazawa, Eiji; Ejima, Akio
CORPORATE SOURCE: Medicinal Chemistry Research Laboratory, Daiichi Pharmaceutical Co., Ltd., Tokyo, 134-8630, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (2002), 50(4), 453-462
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:384813
AB A series of novel 3-substituted-1-[5-methyl-1-(2-pyrimidinyl)-4-pyrazolyl]-1-trans-propenes in order to improve the in vitro and in vivo activity of our prototype 3-[4-(3-chlorophenyl)-1-piperazinyl]-1-[5-methyl-1-(2-pyrimidinyl)-4-pyrazolyl]-1-trans-propene (I) were synthesized and evaluated by assays of growth inhibition against several tumor cell lines in vitro and antitumor activity against some tumor models when dosed both i.p. and orally in vivo. The 3,5-difluorophenyl and 3,5-dichlorophenyl





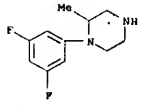
analogs of I showed significantly more potent cytotoxicity than I in vitro and potent antitumor activities without causing decrease of body temperature related to side effects.
IT 475653-33-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and optimization of phenylpiperazine moiety of novel pyrimidinyl pyrazole derivs. in relation to their antitumor activities)
RN 475653-33-9 CAPLUS
CN Pyrimidine, 2-[4-[(1E)-3-[4-(3,5-difluorophenyl)-3-methyl-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



● HCl

IT 475653-31-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and optimization of phenylpiperazine moiety of novel pyrimidinyl pyrazole derivs. in relation to their antitumor activities)
RN 475653-31-7 CAPLUS
CN Piperazine, 1-(3,5-difluorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:293657 CAPLUS
DOCUMENT NUMBER: 136:310065
TITLE: Preparation of substituted piperazine-condensed

morphinoid derivatives as selective δ-opioid agonists and antagonists for treatment of conditions involving δ-opioid receptors

INVENTOR(S): Dondio, Giulio; Gagliardi, Stefania; Graziani, Davide; Raveglia, Luca Francesco

PATENT ASSIGNEE(S): Glaxosmithkline S.P.A., Italy

SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002030935 | A1 | 20020418 | WO 2001-EP11558 | 20011005 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002024772 | A5 | 20020422 | AU 2002-24772 | 20011005 <-- |
| EP 1326868 | A1 | 20030716 | EP 2001-986688 | 20011005 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004511486 | T | 20040415 | JP 2002-534121 | 20011005 |
| US 2004067959 | A1 | 20040408 | US 2003-398313 | 20031003 |

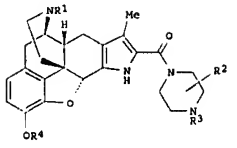
PRIORITY APPLN. INFO.: GB 2000-25056 A 20001012
WO 2001-EP11558 W 20011005

OTHER SOURCE(S): MARPAT 136:310065

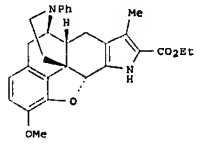
GI







I



II

AB Substituted piperazine-condensed morphinoid derivs. I (R1 = H or alkyl; R2 = H or one or more alkyl groups; R3 is R or RX-; wherein R is H or optionally substituted alkyl, aryl, arylalkyl, cycloalkyl or heterocyclyl and X is a linking group; and R4 = H or alkyl; when R4 = Me and R3 = Me or hydroxyethyl then R2 is not H) were prepared as selective δ-opioid agonists and antagonists. Thus hydrocodeinone was treated with 3-oxo-2-(phenylhydrazono)butyric acid Et ester to give II. II was converted to the acid chloride which reacted with 4-chlorophenylpiperazine HCl to give derivative I (R1 = R4 = Me, R2 = H, R3 = 4-ClC6H4). The activity of the prepared compds. as selective δ-opioid receptor ligands was evaluated in radioligand binding assays using cloned human δ, μ and κ opioid receptors expressed in HEK cells (no data). The most potent compds. showed affinities for the δ receptor ranging from 0.3 to 10 nM with delta selectivity ranging from 15 to 400 times in respect to the other opioid receptor types (no data).

IT 409305-16-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted piperazine-condensed morphinoid derivs. as selective δ-opioid agonists and antagonists)

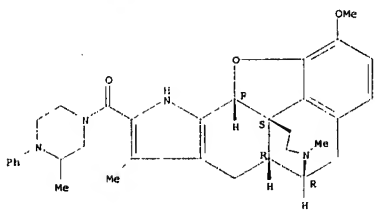
RN 409305-16-4 CAPLUS

CN Piperazine, 2-methyl-4-[[(4bS,8R,8aR,12bR)-5,6,7,8,8a,9,12,12b-octahydro-1-methoxy-7,10-dimethyl-4,8-methanobenzofuro[3,2-e]pyrrolo[2,3-g]isoquinolin-11-yl]carbonyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.







IT 2946-76-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted piperazine-condensed morphinoid derivs. as selective δ-opioid agonists and antagonists)

RN 2946-76-1 CAPLUS

CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:142707 CAPLUS

DOCUMENT NUMBER: 136:200181

TITLE: Substituted and/or fused pyrazoles, particularly piperazinylpropyl-substituted pyrazolopyridines, useful as cathepsin S inhibitors, and their pharmaceutical compositions and use as immunosuppressants

INVENTOR(S): Breitenbucher, J. Guy; Cai, Hui; Edwards, James P.; Grice, Cheryl A.; Gustin, Darin J.; Khatuya, Haripada; Meduna, Steven P.; Pio, Barbara A.; Tays, Kevin L.; Wei, Jianmei

PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA

SOURCE: PCT Int. Appl., 161 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002014314 | A2 | 20020221 | WO 2001-US25289 | 20010810 <-- |
| WO 2002014314 | A3 | 20020606 | | |





| | | | | |
|---|---|---|---|---|
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2419540 | A1 | 20020221 | CA 2001-2419540 | 20010810 <-- |
| AU 200181255 | A | 20020225 | AU 2001-81255 | 20010810 <-- |
| US 2002040020 | A1 | 20020404 | US 2001-928122 | 20010810 <-- |
| EP 1309591 | A2 | 20030514 | EP 2001-959731 | 20010810 |
| EP 1309591 | B1 | 20070124 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004512272 | T | 20040422 | JP 2002-519454 | 20010810 |
| NZ 524193 | A | 20041224 | NZ 2001-524193 | 20010810 |
| RU 2286343 | C2 | 20061027 | RU 2003-107018 | 20010810 |
| AT 352552 | T | 20070215 | AT 2001-959731 | 20010810 |
| MX 2003PA01421 | A | 20040126 | MX 2003-PA1421 | 20030214 |
| IN 2003KN00189 | A | 20050311 | IN 2003-KN189 | 20030214 |
| ZA 2003002052 | A | 20040623 | ZA 2003-2052 | 20030313 |
| US 2007004754 | A1 | 20070104 | US 2006-517040 | 20060907 |
| US 2007004755 | A1 | 20070104 | US 2006-517145 | 20060907 |
| US 2007004738 | A1 | 20070104 | US 2006-517171 | 20060907 |
| US 2007004747 | A1 | 20070104 | US 2006-517518 | 20060907 |
| US 2007010530 | A1 | 20070111 | US 2006-517062 | 20060907 |
| US 2007021437 | A1 | 20070125 | US 2006-517212 | 20060907 |

PRIORITY APPLN. INFO.: US 2000-225138P P 20000814
US 2001-928122 A 20010810
WO 2001-US25289 W 20010810

OTHER SOURCE(S): MARPAT 136:200181

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

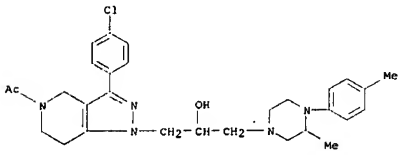
AB Substituted pyrazoles I, methods of manufacturing them, compns. containing them, and
methods of using them to treat, for example, autoimmune diseases mediated by cathepsin S, are described [R1 = H, N3, halo, alkoxy, OH, alkyl, alkenyl, cyano, NO2, (un)substituted NH2, acyl, etc.; R2 = H, halo, alkoxy, alkyl, alkenyl, haloalkyl, cyano, or (un)substituted NH2; or R1R2 = atoms to form (un)substituted (un)saturated (non)aromatic 5- to 7-membered carbo- or heterocyclic ring; R3, R4 = H, alkyl; R5, R6 = H, alkyl, alkenyl, alkoxy, alkylthio, halo, or 4- to 7-membered carbo- or heterocyclyl; or R5R6 = atoms to form (un)substituted (un)saturated (non)aromatic
5- to 7-membered carbo- or heterocyclic ring; n = 1 or 2; Q = (un)substituted C3-6 alkanediyl or alkenediyl (substituents = OH, halo, oxo, aminoalkyl, etc.); X, Y, Z = N, (un)substituted CH; Ar = (un)substituted mono- or bicyclic (hetero)aryl; W = SO2, CO, (un)substituted CH2, bond; or WR1 = atoms to form a benzoxazol-2-yl, benzothiazol-2-yl, benzimidazol-2-yl, 1,2-benzisoxazol-3-yl, 1,2-benzisothiazol-3-yl, or 1,1-dioxo-1,2-benzothiazol-3-yl ring, including stereoisomers and pharmaceutically acceptable salts, esters, and

amides]. Claimed usages include treatment of lupus, rheumatoid arthritis, and particularly asthma, and inhibition of tissue transplant rejection. Approx. 250 individual compds. I were prepared and/or claimed, with detailed prepns. given for 24 compds. For instance, 4-(2-chloro-6-methanesulfonylaminophenyl)piperazine-1-carboxylic acid tert-Bu ester (prepared in 4 steps) was deprotected with TFA and coupled with the corresponding epoxide (prepared in several steps) to give title compound II, a preferred compound. In an assay for inhibition of recombinant human cathepsin S in vitro, II had an IC50 of 0.06 μM. Compound III was another of three specifically preferred compds.

IT 400803-62-5P, 1-[3-(4-Chlorophenyl)-1-(2-hydroxy-3-(3-methyl-4-p-tolylpiperazin-1-yl)propyl]-1,4,6,7-tetrahydropyrazolo[4,3-c]pyridin-5-yl]ethanone
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of piperazinylpropyl-substituted pyrazolopyridines and analogs as cathepsin S inhibitors)

RN 400803-62-5 CAPLUS

CN 1H-Pyrazolo[4,3-c]pyridine-1-ethanol, 5-acetyl-3-(4-chlorophenyl)-4,5,6,7-tetrahydro-α-[[3-methyl-4-(4-methylphenyl)-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 10 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:71877 CAPLUS
DOCUMENT NUMBER: 136:134783
TITLE: Preparation of piperazine(or piperidine)-1-carboxamides as CCR5 modulators
INVENTOR(S): Bondinell, William E.; Neeb, Michael J.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002005819 | A1 | 20020124 | WO 2001-US22529 | 20010713 <-- |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,





RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| AU 2001080599 | A5 | 20020130 | AU 2001-80599 | 20010713 <-- |
| EP 1313477 | A1 | 20030528 | EP 2001-958995 | 20010713 |

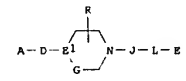
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

| | | | | |
|---|---|---|---|---|
| US 2004038982 | A1 | 20040226 | US 2003-343880 | 20030205 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 2000-218509P | P | 20000715 |
| WO 2001-US22529 | W | 20010713 |

OTHER SOURCE(S): MARPAT 136:134783
GI



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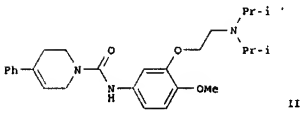


II

AB The title compds. (I; the basic N atom in moiety E may be optionally quaternized with alkyl or optionally present as the N-oxide; A = (un)substituted (hetero)aryl or (hetero)aryl fused to a saturated or partly unsatd. 5-7 membered ring; D = a bond, CO, SO2, etc.; E10 = NC(R26)2, NC(R26)2C(R26)2, CR27C(R26)2, C:CR26; R26 = H, alkyl; R27 = H, CN, NO2, etc.; R = H, alkyl, O; J = CO, SO2; L = NR30, O, C(R30)2; R30 = H, alkyl; E = 3-(2-diisopropylamino)ethoxy-4-methoxyphenyl, etc.] which are modulators, agonists or antagonists, of the CCR5 receptor, and therefore are useful in the treatment and prevention of disease states mediated by CCR5, including, but not limited to, asthma and atopic disorders (for example, atopic dermatitis and allergies), rheumatoid arthritis, sarcoidosis, or idiopathic pulmonary fibrosis and other fibrotic diseases, atherosclerosis, psoriasis, autoimmune diseases such as multiple sclerosis, treating and/or preventing rejection of transplanted organs, and inflammatory bowel disease, were prepared. Thus, treating 4-phenyl-1,2,3,6-tetrahydropyridine.HCl with triphosgene in the presence of Et3N in CH2Cl2 followed by addition of 3-(2-diisopropylamino)ethoxy-4-methoxyaniline afforded II. The compds. I showed CCR5 receptor modulator activity having IC50 values in the range of 0.0001-100 μM. Furthermore, since CD8+ T cells have been implicated in COPD, CCR5 may play a role in their recruitment and therefore antagonists to CCR5 could



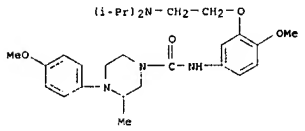


provide potential therapeutic in the treatment of COPD. Also, since CCR5 is a co-receptor for the entry of HIV into cells, selective receptor modulators may be useful in the treatment of HIV infection.

IT 391881-79-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine(or piperidine)-1-carboxamides as CCR5 modulators)

RN 391881-79-1 CAPLUS

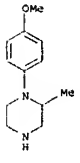
CN 1-Piperazinecarboxamide, N-[3-[2-[bis(1-methylethyl)amino]ethoxy]-4-methoxyphenyl]-4-(4-methoxyphenyl)-3-methyl- (9CI) (CA INDEX NAME)



IT 35947-12-7, 1-(4-Methoxyphenyl)-3-methylpiperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperazine(or piperidine)-1-carboxamides as CCR5 modulators)

RN 35947-12-7 CAPLUS

CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:886128 CAPLUS
DOCUMENT NUMBER: 136:20084
TITLE: Preparation of 5-amino-pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines as adenosine A2a receptor antagonists
INVENTOR(S): Neustadt, Bernard R.; Lindo, Neil A.; Greenlee, William J.; Tulshian, Deen; Silverman, Lisa S.; Xia, Yan; Boyle, Craig D.; Chackalamannil, Samuel
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 66 pp.





CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001092264 | A1 | 20011206 | WO 2001-US16954 | 20010524 <-- |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| CA 2410237 | A1 | 20011206 | CA 2001-2410237 | 20010524 <-- |
| US 2002099061 | A1 | 20020725 | US 2001-865071 | 20010524 <-- |
| US 6630475 | B2 | 20031007 | | |
| EP 1283839 | A1 | 20030219 | EP 2001-945991 | 20010524 |
| EP 1283839 | B1 | 20050420 | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

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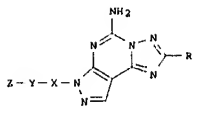
|---|---|---|---|---|
| CN 1451007 | A | 20031022 | CN 2001-813449 | 20010524 |
| JP 2003535094 | T | 20031125 | JP 2002-500877 | 20010524 |
| BR 2001011015 | A | 20050111 | BR 2001-11015 | 20010524 |
| AT 293627 | T | 20050515 | AT 2001-945991 | 20010524 |
| ES 2237576 | T3 | 20050801 | ES 2001-1945991 | 20010524 |
| NZ 522326 | A | 20060331 | NZ 2001-522326 | 20010524 |
| CN 1800186 | A | 20060712 | CN 2006-10004929 | 20010524 |
| HU 200600239 | A2 | 20060728 | HU 2006-239 | 20010524 |
| ZA 2002008898 | A | 20040301 | ZA 2002-8898 | 20021101 |
| NO 2002005651 | A | 20030123 | NO 2002-5651 | 20021125 |
| MX 2002PA11625 | A | 20030327 | MX 2002-PA11625 | 20021125 |
| IN 2002CN01932 | A | 20050211 | IN 2002-CN1932 | 20021125 |
| HK 1049007 | A1 | 20050916 | HK 2003-101315 | 20030221 |
| US 2004023997 | A1 | 20040205 | US 2003-448854 | 20030530 |
| US 6897216 | B2 | 20050524 | | |
| US 2005026932 | A1 | 20050203 | US 2004-912834 | 20040806 |
| US 7067655 | B2 | 20060627 | | |
| JP 2006219497 | A | 20060824 | JP 2006-128415 | 20060502 |
| JP 2007145875 | A | 20070614 | JP 2007-69618 | 20070316 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 2000-207143P | P | 20000526 |
| CN 2001-813449 | A3 | 20010524 |
| JP 2002-500877 | A3 | 20010524 |
| US 2001-865071 | A3 | 20010524 |
| WO 2001-US16954 | W | 20010524 |
| US 2003-448854 | A3 | 20030530 |

OTHER SOURCE(S): MARPAT 136:20084
GI



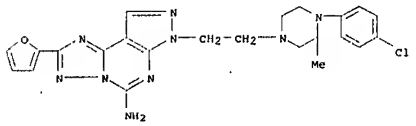
I

AB The title compds. [I; R = (un)substituted Ph, cycloalkenyl, heteroaryl; X = alkylene, COCH2; Y = O, S, CH2S, (CH2)2NH, etc.; Z = (un)substituted Ph, phenylalkyl heteroaryl, etc.; or Z and Y together are substituted piperidinyl or phenyl], useful in the treatment of Parkinson's disease, alone or in combination with other agents for treating Parkinson's disease, were prepared and formulated. E.g., a multi-step synthesis of I [R = 2-furanyl; X = (CH2)2; ZY = 4-(2,4-difluorophenyl)piperazin-1-yl] was described. Compds. I showed Ki of 0.3-57 nM against A2a receptor binding.

IT 377727-38-3P 377727-60-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 5-amino-pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines as adenosine A2a receptor antagonists)

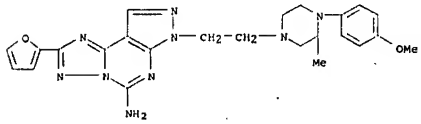
RN 377727-38-3 CAPLUS

CN 7H-Pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-amine, 7-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-2-(2-furanyl)- (9CI) (CA INDEX NAME)



RN 377727-60-1 CAPLUS

CN 7H-Pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-amine, 2-(2-furanyl)-7-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)







REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

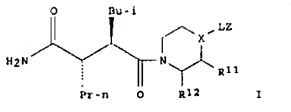
L9 ANSWER 12 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:747771 CAPLUS
DOCUMENT NUMBER: 135:303912
TITLE: Preparation of succinoylamino-heterocycles as Aβ peptide production inhibitors
INVENTOR(S): Thompson, Lorin Andrew; Kasireddy, Padmaja
PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001074796 | A1 | 20011011 | WO 2001-US10297 | 20010330 <-- |
| W: AT, AU, BR, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, HU, IL, IN, JP, KR, LT, LU, LV, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |
| CA 2404314 | A1 | 20011011 | CA 2001-2404314 | 20010330 <-- |
| EP 1268454 | A1 | 20030102 | EP 2001-924498 | 20010330 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR | | | | |
| JP 2003529594 | T | 20031007 | JP 2001-572489 | 20010330 |
| PRIORITY APPLN. INFO.: | | | US 2000-193490P | P 20000331 |
| | | | WO 2001-US10297 | W 20010330 |

OTHER SOURCE(S): MARPAT 135:303912
GI







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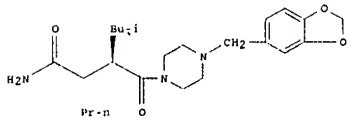


II

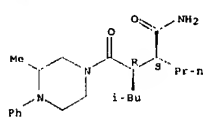
AB Title compds. [I; R11 = H, CH3, LZ, OH, CH2OH, CONH2, COOCH2CH3; R12 = H, LZ; LZ = CH3, CH2C6H5, 2-CH3C6H4, 3-CF3C6H4, 4-FC6H4, CH2CH2OH, CH2CH3, CH2CH:CH2C6H5, 2,6-(CH3)2C6H3, R10; R10 = CH2COOCH2CH3, COCH3, (4-ClC6H4)2CH; X = CH, N, CCOOCH2CH3, CN(CH3)2, COH, CCH3, CCOCH3, CCONH2, CCOCH2CH3, etc.] are prepared and are useful as remedies of neurol. disorders related to β-amyloid production such as Alzheimer's disease and Down's syndrome. Title compds. I inhibit the processing of amyloid precursor protein and, more specifically, inhibit the production of Aβ-peptide, thereby acting to prevent formation of neurol. deposits of amyloid protein. Thus, the title compound II was prepared and in vitro tested for Aβ peptide accumulation inhibition.

IT 365538-73-4P 365539-26-0P 365539-46-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of succinoylaminoheterocycles as Aβ peptide production inhibitors)

RN 365538-73-4 CAPLUS

CN 1-Piperazinebutanamide, 3-methyl-β-(2-methylpropyl)-γ-oxo-4-phenyl-α-propyl-, (αS,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



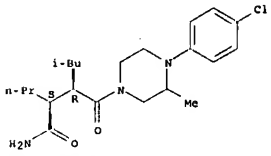




RN 365539-26-0 CAPLUS

CN 1-Piperazinebutanamide, 4-(4-chlorophenyl)-3-methyl-β-(2-methylpropyl)-γ-oxo-α-propyl-, (αS,βR)- (9CI) (CA INDEX NAME)

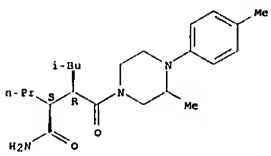
Absolute stereochemistry.



RN 365539-46-4 CAPLUS

CN 1-Piperazinebutanamide, 3-methyl-4-(4-methylphenyl)-β-(2-methylpropyl)-γ-oxo-α-propyl-, (αS,βR)- (9CI) (CA INDEX NAME)

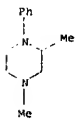
Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

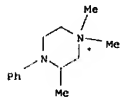
L9 ANSWER 13 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:731861 CAPLUS
DOCUMENT NUMBER: 136:14987
TITLE: Structure-Affinity Relationships of a Unique Nicotinic Ligand: N1-Dimethyl-N4-phenylpiperazinium Iodide (DMPP)
AUTHOR(S): Romanelli, Maria Novella; Manetti, Dina; Scapecchi, Serena; Borea, Pier Andrea; Dei, Silvia; Bartolini, Alessandro; Ghelardini, Carla; Gualtieri, Fulvio; Guandalini, Luca; Varani, Katia
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Firenze, Florence, 50121, Italy
SOURCE: Journal of Medicinal Chemistry (2001), 44(23), 3946-3955
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal
LANGUAGE: English
AB DMPP is a well-known nicotinic agonist that does not fit any proposed pharmacophore for nicotinic binding and represents a unique ligand among the hundreds of nicotinic agonists studied in the past decades. A systematic modulation of the chemical structure of DMPP, aimed to establish its structure-affinity relationships, is reported. The research has allowed to identify mols. with affinities for $\alpha4\beta2$ receptors in the low nanomolar range, some 2 orders of magnitude lower than the lead compound The agonistic properties of the most interesting compds. have been assessed by measuring their analgesic activity on mice (hot-plate test). Another result of the research was the identification of DMPP analogs with Ki = 90 nM and 180 nM, that maintain affinity for the central nicotinic receptor when the ammonium function is changed into an aminic one and are therefore possible leads for drug development in neurodegenerative diseases.
IT 33905-49-6P 378758-81-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(structure-activity relationships of a nicotinic ligand, DMPP)
RN 33905-49-6 CAPLUS
CN Piperazine, 2,4-dimethyl-1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 378758-81-7 CAPLUS
CN Piperazinium, 1,1,3-trimethyl-4-phenyl-, iodide (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

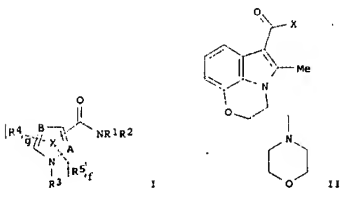
L9 ANSWER 14 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:597958 CAPLUS
DOCUMENT NUMBER: 135:166827
TITLE: Preparation of 1H-indole-3-carboxamides, 1H-indazole-3-carboxamides, 1H-pyrido[4,3-b]indol-1-ones and pyrrolo[1,2,3-de]-1,4-benzoxazine-6-carboxamides as cannabinoid receptor modulators for treating respiratory and non-respiratory diseases
INVENTOR(S): Leftheris, Katerina; Zhao, Rulin; Chen, Bang-Chi; Kiener, Peter; Wu, Hong; Pandit, Chennagiri R.; Wrobleski, Stephen; Chen, Ping; Hynes, John, Jr.; Longphre, Malinda; Norris, Derek J.; Spergel, Steven; Tokarski, John
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA; et al.
SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001058869 | A2 | 20010816 | WO 2001-US4131 | 20010208 <-- |
| WO 2001058869 | A3 | 20020124 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2399791 | A1 | 20010816 | CA 2001-2399791 | 20010208 <-- |
| AU 200134958 | A | 20010820 | AU 2001-34958 | 20010208 <-- |
| EP 1254115 | A2 | 20021106 | EP 2001-907144 | 20010208 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004502642 | T | 20040129 | JP 2001-558420 | 20010208 |
| PRIORITY APPLN. INFO.: | | | US 2000-181818P | P 20000211 |
| | | | WO 2001-US4131 | W 20010208 |
| OTHER SOURCE(S): | MARPAT 135:166827 | | | |

GI





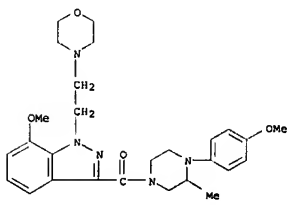


I II

AB The title compds. [I; A, B = C, N so that ring X = pyrrole, pyrazole or imidazole (wherein when A = N, the group CONR1R2 is attached to atom C-3 and R5 does not exist; and when A = C, one of CONR1R2 and R5 is attached to A and the other to atom C-3; and when B = C, two R4 groups attached to B and atom C-5, resp., form a fused 6-membered heteroaryl); f = 0-1; g = 1-2; R1, R2 = H, alkyl, heterocycloalkyl, etc.; R2 together with R1 or R5 forms a 5-6 membered heterocyclo; R3 = H, alkyl, aryl, etc.; R4 is attached to atom C-5 and optionally B and is H, alkyl, aryl, etc.; R5 is attached to A or atom C-3 and is H, alkyl, aryl, etc.; R5 together with R2 forms a heterocyclo], useful as cannabinoid receptor modulators (no data given) for treating respiratory and non-respiratory leukocyte-activation associated diseases, were prepared Thus, reacting the acid chloride II [X = Cl] (multi-step synthesis given) with 2,2,6,6-tetramethylcyclohexylamine afforded the pyrrolo[1,2,3-de]-1,4-benzoxazine-6-carboxamide II [X = 2,2,6,6-tetramethylcyclohexylamino].
IT 354572-38-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1H-indole-3-carboxamides, 1H-indazole-3-carboxamides, 1H-pyrido[4,3-b]indol-1-ones and pyrrolo[1,2,3-de]-1,4-benzoxazine-6-carboxamides as cannabinoid receptor modulators for treating respiratory and non-respiratory diseases)
RN 354572-38-6 CAPLUS
CN Piperazine, 4-[[7-methoxy-1-[2-(4-morpholinyl)ethyl]-1H-indazol-3-yl]carbonyl]-1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)







L9 ANSWER 15 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:581863 CAPLUS
DOCUMENT NUMBER: 135:152801
TITLE: Preparation of 2-benzothiazolyl ureas as protein kinase inhibitors
INVENTOR(S): Cusack, Kevin P.; Scott, Barbara; Arnold, Lee D.; Ericsson, Anna
PATENT ASSIGNEE(S): Basf Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001057008 | A1 | 20010809 | WO 2001-US3803 | 20010206 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2398754 | A1 | 20010809 | CA 2001-2398754 | 20010206 <-- |
| EP 1254123 | A1 | 20021106 | EP 2001-908878 | 20010206 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2001008085 | A | 20030318 | BR 2001-8085 | 20010206 |
| HU 200300359 | A2 | 20030628 | HU 2003-359 | 20010206 |
| JP 2003521543 | T | 20030715 | JP 2001-556958 | 20010206 |
| US 2003153568 | A1 | 20030814 | US 2001-777554 | 20010206 |
| US 7091227 | B2 | 20060815 | | |
| ZA 2002006235 | A | 20040213 | ZA 2002-6235 | 20020805 |
| IN 2002MN01057 | A | 20040529 | IN 2002-MN1057 | 20020805 |
| NO 2002003713 | A | 20021004 | NO 2002-3713 | 20020806 <-- |
| MX 2002PA07632 | A | 20040823 | MX 2002-PA7632 | 20020807 |
| BG 107062 | A | 20030430 | BG 2002-107062 | 20020904 |

PRIORITY APPLN. INFO.: US 2000-180841P P 20000207
WO 2001-US3803 W 20010206

OTHER SOURCE(S): MARPAT 135:152801
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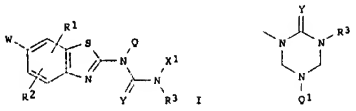
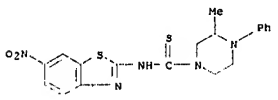


I II

AB The title compds. [I; Q = H or a bond which is taken together with X1 and two N atoms to which Q and X1 are attached and C:Y group to which the two N atoms are attached to form II; Q1 = alkyl; Y = O, S; W = H, Cl, Br, etc.; X1 = H, alkyl, hydroxyalkyl or a bond which is taken together with R3 to form pyrrolidino, piperazino or morpholino; R1, R2 = H, halo, OH, etc.; R3 = H, alkyl, aryl, etc.], useful as inhibitors of serine/threonine and tyrosine kinases such as FGFR, PDGFR, KDR, VEGFR-3, Tie-2, Tie-1, Lck, Fyn, Blk, Lyn, Src, cdc2 (cdk1) or Plk-1 (biol. data given), were prepared and formulated. Thus, reacting 3,5-dimethoxyphenyl isocyanate with 2-amino-6-nitrobenzothiazole in the presence of Et3N in PhMe afforded I [W = NO2; Q, X1, R1, R2 = H; Y = O; R3 = 3,5-(MeO)2C6H3]. In particular, compds. I are useful as inhibitors of tyrosine kinases that are important in hyperproliferative diseases, especially in cancer and in the process of angiogenesis.

IT 352527-26-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-benzothiazolyl ureas as protein kinase inhibitors)

RN 352527-26-5 CAPLUS
CN 1-Piperazinecarbothioamide, 3-methyl-N-(6-nitro-2-benzothiazolyl)-4-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 16 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:472725 CAPLUS
DOCUMENT NUMBER: 135:76897
TITLE: Synthesis and use of substituted piperidine and piperazine derivatives (e.g. N-(sulfonyl)aryl, N-alkylcarboxamido piperazines) as antagonists of the





P2X7 receptor
INVENTOR(S): Meghani, Premji; Bennion, Colin
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 156 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001046200 | A1 | 20010628 | WO 2000-SE2580 | 20001218 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2394095 | A1 | 20010628 | CA 2000-2394095 | 20001218 <-- |
| BR 2000016543 | A | 20020917 | BR 2000-16543 | 20001218 <-- |
| EP 1242427 | A1 | 20020925 | EP 2000-989102 | 20001218 <-- |
| EP 1242427 | B1 | 20030813 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2003518126 | T | 20030603 | JP 2001-547110 | 20001218 |
| AT 247123 | T | 20030815 | AT 2000-989102 | 20001218 |
| NZ 519498 | A | 20040227 | NZ 2000-519498 | 20001218 |
| AU 776592 | B2 | 20040916 | AU 2001-25648 | 20001218 |
| ZA 2002004307 | A | 20030829 | ZA 2002-4307 | 20020529 |
| US 2003013721 | A1 | 20030116 | US 2002-168094 | 20020617 |
| US 6969713 | B2 | 20051129 | | |
| NO 2002003037 | A | 20020822 | NO 2002-3037 | 20020621 <-- |
| MX 2002PA06261 | A | 20021205 | MX 2002-PA6261 | 20020621 <-- |
| US 2005272745 | A1 | 20051208 | US 2005-125335 | 20050510 |

PRIORITY APPLN. INFO.: SE 1999-4738 A 19991222
WO 2000-SE2580 W 20001218
US 2002-168094 A1 20020617

OTHER SOURCE(S): MARPAT 135:76897
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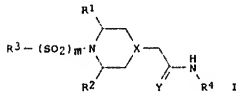

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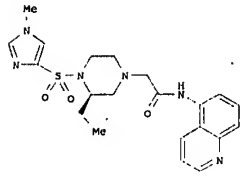


II

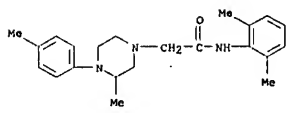
AB Compds. of formula I, their preparation and use as P2X7 receptor antagonists are claimed [wherein: X = N or CR5; Y = O, S, or NR6; R1, R2 = H or alkyl but do not simultaneously represent H, or R1R2 = CH2ZCH2; Z = bond, O, S, CH2, or NR7; m = 0 or 1; R3 = 5-10 membered unsatd. (substituted) ring which may contain 1-4 heteroatoms chosen from N, O or S; R4 = ortho-substituted Ph/pyridinyl, said rings may be further substituted, or R4 = 9-10 membered unsatd. (substituted) bicyclic ring system which may contain 1-4 heteroatoms chosen from N, O or S; R5 = H, OH or alkoxy; R6 = H, CN, NO2, OH, alkyl or alkoxy; R7 = H, alkyl; with addnl. provisos]. More than 100 synthetic examples are provided. For instance, (R)-3-ethyl-1-phenylmethylpiperazine (prepared in 3 steps from (R)-N-Boc-2-aminobutyric acid) was reacted with 1-methylimidazole-4-sulfonyl chloride in the presence of base to give the corresponding N-benzyl piperazine sulfonamide. This intermediate was debenzylated and reacted with 2-chloro-N-(quinolin-5-yl)acetamide to yield II. The invention compds. were tested for antagonist activity at the P2X7 receptor using benzoylbenzoyl ATP (bbATP, a P2X7 agonist) as a control for P2X7 receptor activation. Compds. of the invention had pIC50 (neg. log of the concentration of test compound necessary to reduce the bbATP agonist activity by 50%) > 5.0. Compds. I are used for treatment of rheumatoid arthritis and COPD, and for effecting immunosuppression.

IT 347194-32-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; synthesis and use of substituted piperidine and piperazine derivs. (e.g. N-(sulfonyl)aryl, N-alkylcarboxamido piperazines) as antagonists of the P2X7 receptor)

RN 347194-32-5 CAPLUS
CN 1-Piperazineacetamide, N-(2,6-dimethylphenyl)-3-methyl-4-(4-methylphenyl)- (9CI) (CA INDEX NAME)

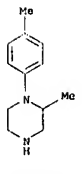






IT 35947-11-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(precursor; synthesis and use of substituted piperidine and piperazine derivs. (e.g. N-(sulfonyl)aryl, N-alkylcarboxamido piperazines) as antagonists of the P2X7 receptor)

RN 35947-11-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)- (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 . ANSWER 17 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:338558 CAPLUS
DOCUMENT NUMBER: 134:340709
TITLE: Preparation of substituted dipeptides having NOS inhibiting activity
INVENTOR(S): Shima, Ichiro; Ohkawa, Takehiko; Ohne, Kazuhiko; Sato, Kentaro; Ishibashi, Naoki; Imamura, Kenichiro
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001032690 | A1 | 20010510 | WO 2000-JP7579 | 20001027 <-- |
| W: BR, CA, CN, JP, KR, US | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| EP 1226159 | A1 | 20020731 | EP 2000-970164 | 20001027 <-- |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY

| | | | | | |
|---|---|---|---|---|---|
| JP 2003513104 | T | 20030408 | JP 2001-535389 | | 20001027 |
| US 6825200 | B1 | 20041130 | US 2002-111412 | | 20020506 |
| PRIORITY APPLN. INFO.: | | | AU 1999-3868 | A | 19991104 |
| | | | WO 2000-JP7579 | W | 20001027 |

OTHER SOURCE(S): MARPAT 134:340709

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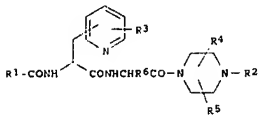


I

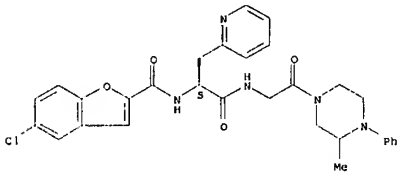
AB Dipeptides I [R1 is benzofuranyl or styryl substituted by halogen; R2 is (un)substituted Ph, pyridyl, thienyl, or thiazolyl; R3, R5 = H or lower alkoxy; R4, R5 = H, lower alkyl or optionally protected hydroxy(lower)alkyl] or their pharmaceutically acceptable salts were prepared for use in the prevention and/or treatment of nitric oxide-mediated diseases. Thus, 5-chloro-N-[(1S)-2-[[2-[4-(4-chlorophenyl)-1-piperazinyl]-2-oxoethyl]amino]-2-oxo-1-(2-pyridylmethyl)ethyl]-1-benzofuran-2-carboxamide (II) was prepared via amidation reaction and showed 100% inhibition of nitric acid. The combination of compound II and FK507 dramatically prolonged graft survival in rat cardiac allograft.

IT 337530-63-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted dipeptides having NOS inhibiting activity)

RN 337530-63-9 CAPLUS

CN 2-Pyridinepropanamide, α-[[(5-chloro-2-benzofuranyl)carbonyl]amino]-N-[2-(3-methyl-4-phenyl-1-piperazinyl)-2-oxoethyl]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.







SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|
| DE 19945594 | A1 | 20010329 | DE 1999-19945594 | 19990923 <-- |
| CA 2388759 | A1 | 20010329 | CA 2000-2388759 | 20000919 <-- |
| EP 1228053 | A1 | 20020807 | EP 2000-969264 | 20000919 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2003509505 | T | 20030311 | JP 2001-524983 | 20000919 |
| JP 3908034 | B2 | 20070425 | | |
| MX 2002PA02838 | A | 20030721 | MX 2002-PA2838 | 20020314 |
| US 6818644 | B1 | 20041116 | US 2002-89024 | 20020701 |
| PRIORITY APPLN. INFO.: | | | DE 1999-19945594 | A 19990923 |
| | | | WO 2000-EP9146 | W 20000919 |

OTHER SOURCE(S): MARPAT 134:266313

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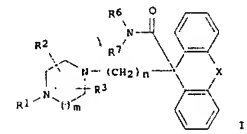

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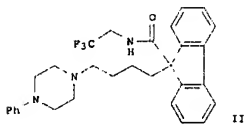


II

AB Compds. of formula I [wherein; n is 1-5; m is 1 or 2; X is a bond, O, CH2(CH2), imino or N-alkyl-imino; R1 is (substituted) aryl or heteroaryl; R2, R3 are hydrogen or alkyl; R6, R7 are H, (fluoro)alkyl, cycloalkyl, Ph, heteroaryl, etc., or NR6R7 may form a 3-7 membered ring.]. Thirty eight examples of I are prepared (e.g. II). Compound II was prepared by alkylation of 9-fluorenecarboxylic acid with 1,4-dibromobutane. The alkylated intermediate was converted to its acyl chloride derivative, and treated with 2,2,2-trifluoroethylamine to provide pivotal intermediate, 9-(4-bromobutyl)-9H-fluorene-9-(2,2,2-trifluoroethylcarboxamide). Alkylation of 1-phenylpiperazine with this intermediate yields II. Three solid oral dosage formulations of compds. I are disclosed. Compds. of

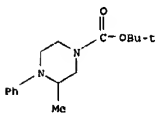




IT 337530-61-7P 337530-62-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted dipeptides having NOS inhibiting activity)

RN 337530-61-7 CAPLUS

CN 1-Piperazinecarboxylic acid, 3-methyl-4-phenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 337530-62-8 CAPLUS

CN Piperazine, 2-methyl-1-phenyl-, hydrochloride (9CI) (CA INDEX NAME)

●x HCl

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 18 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:228874 CAPLUS

DOCUMENT NUMBER: 134:266313

TITLE: Preparation and use of substituted piperazine derivatives as MTP inhibitors

INVENTOR(S): Lehmann-Lintz, Thorsten; Heckel, Armin; Thomas, Leo; Mark, Michael

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001021604 | A1 | 20010329 | WO 2000-EP9146 | 20000919 <-- |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,





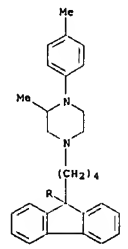
formula I are said to be inhibitors of the microsomal triglyceride-transfer protein (MTP). Use of compds. I to prepare drugs which lower plasma levels of atherogenic lipoproteins is claimed.

IT 331767-25-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and use of substituted piperazine derivs.)

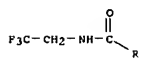
RN 331767-25-0 CAPLUS

CN 9H-Fluorene-9-carboxamide, 9-[4-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]butyl]-N-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 19 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:208282 CAPLUS

DOCUMENT NUMBER: 134:237472

TITLE: Preparation of 1-amino-3-thienoisoxazolylphenoxy-2-propanols as dopamine D4 antagonists

INVENTOR(S): Fink, David M.; Freed, Brian S.; Hrib, Nicholas J.; Kosley, Raymond W., Jr.; Lee, George E.; Merriman, Gregory N.; Rauckman, Barbara S.

PATENT ASSIGNEE(S): Aventis Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 157 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001019833 | A1 | 20010322 | WO 2000-US24962 | 20000913 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2383340 | A1 | 20010322 | CA 2000-2383340 | 20000913 <-- |
| BR 2000014515 | A | 20020625 | BR 2000-14515 | 20000913 <-- |
| EP 1216250 | A1 | 20020626 | EP 2000-964969 | 20000913 <-- |
| EP 1216250 | B1 | 20031119 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| HU 200203526 | A2 | 20030128 | HU 2002-3526 | 20000913 |
| EE 200200135 | A | 20030415 | EE 2002-135 | 20000913 |
| AT 254621 | T | 20031215 | AT 2000-964969 | 20000913 |
| PT 1216250 | T | 20040430 | PT 2000-964969 | 20000913 |
| ES 2209995 | T3 | 20040701 | ES 2000-964969 | 20000913 |
| TW 530060 | B | 20030501 | TW 2000-89118850 | 20000914 |
| NO 2002001251 | A | 20020510 | NO 2002-1251 | 20020313 <-- |
| MX 2002PA02695 | A | 20020730 | MX 2002-PA2695 | 20020313 <-- |
| ZA 2002001762 | A | 20030602 | ZA 2002-1762 | 20020321 |
| US 7125903 | B1 | 20061024 | US 2002-88250 | 20021223 |
| US 2007004695 | A1 | 20070104 | US 2006-459068 | 20060721 |
| PRIORITY APPLN. INFO.: | | | US 1999-396081 | A1 19990914 |
| | | | US 1999-229355P | P 19990914 |
| | | | WO 2000-US24962 | W 20000913 |
| | | | US 2002-88250 | A3 20021223 |

OTHER SOURCE(S): MARPAT 134:237472

AB RZOCH2CR1R2CH2NR3R4 [I; R = e.g., thieno[2,3-d]isoxazol-3-yl; R1 = OH or alkoxy; R2,R4 = H or alkyl; R3 = CH2R5, CH2CH(OH)R5, indanyl, etc.; R5 = cyclohex(en)yl, (hetero)aryl, etc.; Z = phenylene] were prepared Thus, 3-bromothiophene was acylated by 3-(MeO)C6H4COCl and the oximated product cyclized to give, after O-demethylation, 3-RC6H4OH [R = thieno[2,3-d]isoxazol-3-yl] which was etherified by (R)-glycidyl tosylate and the product aminated by PhCHMeNH2 to give (R)-3-RC6H4OCH2CH(OH)CH2NMeCH2Ph (R as above). Data for biol. activity of I were given.

IT 330651-02-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-amino-3-thienoisoxazolylphenoxy-2-propanols as dopamine D4 antagonists)

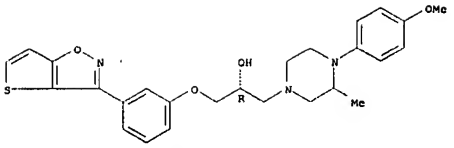
RN 330651-02-0 CAPLUS

CN 1-Piperazineethanol, 4-(4-methoxyphenyl)-3-methyl- α-[(3-thieno[2,3-d]isoxazol-3-ylphenoxy)methyl]-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



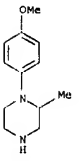




IT 35947-12-7, 1-(4-Methoxyphenyl)-2-methylpiperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 1-amino-3-thienoisoxazolylphenoxy-2-propanols as dopamine D4 antagonists)

RN 35947-12-7 CAPLUS

CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 20 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:115118 CAPLUS
DOCUMENT NUMBER: 134:163065
TITLE: Preparation of hydroxamic acid and N-formyl hydroxylamine derivatives as antibacterial agents
INVENTOR(S): Pratt, Lisa Marie; Keavey, Kenneth Noel; Pain, Gilles Denis; Mounier, Laurent Franck
PATENT ASSIGNEE(S): British Biotech Pharmaceuticals Limited, UK
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001010834 | A2 | 20010215 | WO 2000-GB3078 | 20000810 <-- |
| WO 2001010834 | A3 | 20010628 | | |
| W: AE, AU, BR, BY, CA, CN, CZ, DZ, EE, GB, GE, HU, ID, IL, IN, IS, JP, KE, KR, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, US, VN, ZA, ZW | | | | |





| | | | | |
|---|---|---|---|---|
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CN 1373754 | A | 20000810 | CN 2000-812860 | 20000810 <-- |
| CA 2379061 | A1 | 20010215 | CA 2000-2379061 | 20000810 <-- |
| EP 1202968 | A2 | 20020508 | EP 2000-949820 | 20000810 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY | | | | |
| BR 2000013112 | A | 20020611 | BR 2000-13112 | 20000810 <-- |
| TR 200200360 | T2 | 20020621 | TR 2002-360 | 20000810 <-- |
| HU 200202514 | A2 | 20021128 | HU 2002-2514 | 20000810 <-- |
| JP 2003506438 | T | 20030218 | JP 2001-515301 | 20000810 |
| AU 766881 | B2 | 20031023 | AU 2000-63080 | 20000810 |
| NZ 517239 | A | 20040924 | NZ 2000-517239 | 20000810 |
| CN 1704402 | A | 20051207 | CN 2005-10081198 | 20000810 |
| RU 2269525 | C2 | 20060210 | RU 2002-106409 | 20000810 |
| CN 101007784 | A | 20070801 | CN 2007-10007364 | 20000810 |
| ZA 2002001093 | A | 20030507 | ZA 2002-1093 | 20020207 |
| NO 2002000621 | A | 20020409 | NO 2002-621 | 20020208 <-- |
| MX 2002PA01394 | A | 20020812 | MX 2002-PA1394 | 20020208 <-- |
| US 6846825 | B1 | 20050125 | US 2002-49131 | 20020710 |
| US 2005065095 | A1 | 20050324 | US 2004-953788 | 20040930 |
| US 7186719 | B2 | 20070306 | | |
| PRIORITY APPLN. INFO.: | | | GB 1999-18869 | A 19990810 |
| | | | GB 1999-27093 | A 19991116 |
| | | | CN 2000-812860 | A3 20000810 |
| | | | WO 2000-GB3078 | W 20000810 |
| | | | US 2002-49131 | A3 20020710 |

OTHER SOURCE(S): MARPAT 134:163065

AB Selected compds. QCH(R1)CH(R2)C(O)A (I) and pharmaceutical and veterinary compns. comprising such compds. are antibacterial agents with respect to a range of Gram-pos. and Gram-neg. organisms. In I, Q = -N(OH)C(O)H or -C(O)NH(OH); R1 = H, C1-C6 alkyl or C1-C6 alkyl substituted by ≥ halogen atoms, or, except when Q is -N(OH)C(O)H, hydroxy, C1-C6 alkoxy, C1-C6 alkenyloxy, amino, C1-C6 alkylamino, or di-(C1-C6 alkyl)amino; R2 = substituted or unsubstituted C1-C6 alkyl, cycloalkyl(C1-C6 alkyl)- or aryl(C1-C6 alkyl)-; and A = -NHCHR4C(O)NR5R6 or -NR5R6, wherein R4 = side chain of a natural or non-natural α-amino acid, and R5 and R6 when taken together with the N atom to which they are attached form a saturated heterocyclic 1st ring of 5 to 7 atoms (piperidine and piperazine in the examples). In general, the compds. of the examples are more active against the Gram pos. S. capitis than the Gram neg. E. coli. Test results are also reported for 2R-cyclopentylmethyl-3-(formylhydroxyamino)-N-(1S-[4-[4-(4-hydroxypiperidine-1-carbonyl)phenoxy]piperidine-1-carbonyl]-2,2-dimethylpropyl)propionamide against certain respiratory tract pathogens. Although the methods of preparation are not claimed, ,apprx.95 example prepns. are included.

IT 325795-50-4P, 2R-[(Formylhydroxyamino)methyl]hexanoic acid (1S-[4-(4-methoxyphenyl)-3-methylpiperazine-1-carbonyl]-2,2-dimethylpropyl)amide 325795-56-0P, N-Hydroxy-N-{2R-[4-(4-methoxyphenyl)-3-methylpiperazine-1-carbonyl]hexyl}formamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of hydroxamic acid and N-formyl hydroxylamine derivs. as antibacterial agents)

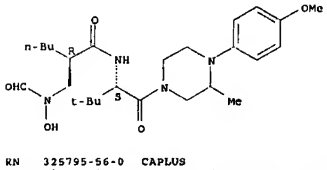
RN 325795-50-4 CAPLUS

CN Hexanamide, 2-[(formylhydroxyamino)methyl]-N-[(1S)-1-[[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]carbonyl]-2,2-dimethylpropyl]-, (2R)- (9CI) (CA INDEX NAME)





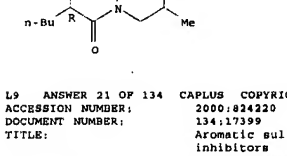
Absolute stereochemistry.



RN 325795-56-0 CAPLUS

CN Piperazine, 4-[(2R)-2-[[(formylhydroxyamino)methyl]-1-oxohexyl]-1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



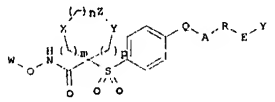
L9 ANSWER 21 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:824220 CAPLUS
DOCUMENT NUMBER: 134:17399
TITLE: Aromatic sulfone hydroxamic acid metalloprotease inhibitors
INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Boehm, Terri L.; Carroll, Jeffrey N.; Decrescenzo, Gary A.; Fobian, Yvette M.; Freskos, John N.; Getman, Daniel P.; McDonald, Joseph J.; Hockerman, Susan L.; Howard, Susan C.; Kolodziej, Stephen A.; Li, Madeleine Hui; Mischke, Deborah A.; Rico, Joseph G.; Stehle, Nathan W.; Tollefson, Michael B.; Vernier, William F.; Villamil, Clara I.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 616 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000069821 | A1 | 20001123 | WO 2000-US6719 | 20000515 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, | | | | |

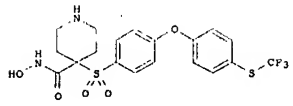
CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| US 6750228 | B1 | 20040615 | US 2000-570731 | | 20000512 |
| CA 2372934 | A1 | 20001123 | CA 2000-2372934 | | 20000515 <-- |
| EP 1183239 | A1 | 20020306 | EP 2000-930088 | | 20000515 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | | |
| BR 2000010562 | A | 20030610 | BR 2000-10562 | | 20000515 |
| JP 2003520196 | T | 20030702 | JP 2000-618238 | | 20000515 |
| AU 766792 | B2 | 20031023 | AU 2000-47970 | | 20000515 |
| NZ 515217 | A | 20040430 | NZ 2000-515217 | | 20000515 |
| ZA 2001009006 | A | 20021202 | ZA 2001-9006 | | 20011031 <-- |
| NO 2001005543 | A | 20020110 | NO 2001-5543 | | 20011113 <-- |
| MX 2001PA11569 | A | 20050620 | MX 2001-PA11569 | | 20011113 |
| PRIORITY APPLN. INFO.: | | | US 1999-311837 | A | 19990514 |
| | | | US 2000-570731 | A | 20000512 |
| | | | US 1997-66007P | P | 19971114 |
| | | | US 1998-95347P | P | 19980804 |
| | | | US 1998-101080P | P | 19980918 |
| | | | US 1999-256948 | B2 | 19990224 |
| | | | WO 2000-US6719 | W | 20000515 |

OTHER SOURCE(S): MARPAT 134:17399
GI



I

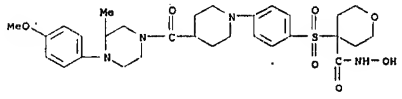


II

AB A treatment process is disclosed that comprises administering an effective amount of an aromatic sulfone hydroxamic acid I [W = H, cation, certain acyl or thioacyl groups; m, n, p = 0-2; (m+n+p) = 1 to 4; one of X, Y, and Z = CO, NH or derivs., O, S, SO, SO2, etc., and the other two = (un)substituted CH2; or XZ or ZY = (un)substituted NHCO, NHSO, NHSO2, SS, OCO, etc., and the other one = (un)substituted CH2; or n = 0 and XZY = atoms to complete various N/O/S heterocycles; Q = 5- to 7-membered heterocycle with 1-2 N atoms, one bound to Ph, and with -AREY bound in para-type positions; A = bond, O, S, (un)substituted NH, COO, OCO, CH:CH, C.tplbond.C, N:N, NHNH, NHCOO, (un)substituted CONH, NHCO, etc.; R = alkylene, arylene, heteroarylene, etc., with provisos; E = bond, CONH, NHCO, CO, SO2, NHSO2, SO2NH, S, etc.; Y = absent, H, alkyl, alkoxy, aryl, aryloxy, heteroaryl, etc.] to a host having a condition associated with pathol. matrix metalloprotease (MMP) activity. I exhibit excellent inhibitory activity of one or more MMP enzymes, such as MMP-2, MMP-9 and MMP-13, while exhibiting substantially less inhibition of (at least) MMP-1. Also disclosed are metalloprotease inhibitor compds. having such selective activities, processes for manufacture of such compds., and pharmaceutical compns. using such inhibitors. The compds. are potentially useful against a wide variety of conditions, notably as antiinflammatory, antiangiogenesis, and antitumor agents. Over 900 example compds. are listed, most with supporting phys. data, and many with synthetic details. For instance, Et N-(tert-butoxycarbonyl)-4-(4-fluorophenylsulfonyl)-4-piperidinecarboxylate (preparation given) was subjected to a sequence of: (1) etherification with 4-(CF3S)C6H4OH (100%); (2) alkaline hydrolysis of the ester (100%); (3) amidation with THP-ONH2 (45%); and (4) acid deprotection of the THP ether (40%), to give title compound II.HCl. The latter salt selectively inhibited MMP-13 with IC50 0.2 nM, and MMP-2 with IC50 0.1 nM, but with IC50 >10,000 nM against MMP-1.

IT 308821-73-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of aromatic sulfone hydroxamic acids as metalloprotease inhibitors)

RN 308821-73-0 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[4-[[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]carbonyl]-1-piperidinyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

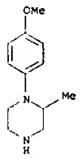


IT 35947-12-7, 1-(4-Methoxyphenyl)-2-methylpiperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of aromatic sulfone hydroxamic acids as metalloprotease inhibitors)

RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)







REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 22 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:628119 CAPLUS
DOCUMENT NUMBER: 133:222745
TITLE: Preparation of 1-[(2-arylindol-3-yl)-1-oxoalkyl]piperazines as antagonists of tachykinins
INVENTOR(S): Chapman, Kevin T.; Dinnell, Kevin; Elliott, Jason Matthew; Hollingworth, Gregory John; Hutchins, Steven Michael; Shaw, Duncan Edward; Willoughby, Christopher Alan
PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000051984 | A1 | 20000908 | WO 2000-GB650 | 20000223 <-- |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6518273 | B1 | 20030211 | US 2001-914893 | 20010904 |
| PRIORITY APPLN. INFO.: | | | GB 1999-5010 | A 19990304 |
| | | | WO 2000-GB650 | W 20000223 |

OTHER SOURCE(S): MARPAT 133:222745
GI





bond, O, S, (un)substituted NH, COO, OCO, CH:CH, C.tplbond.C, N:N, NHNH, NHCOO, (un)substituted CONH, NHCO, etc.; R = alkylene, arylene, heteroarylene, etc., with provisos; E = bond, CONH, NHCO, CO, SO2, NHSO2, SO2NH, S, etc.; Y = absent, H, alkyl, alkoxy, aryl, aryloxy, heteroaryl, etc.] to a host having a condition associated with pathol. matrix metalloprotease (MMP) activity. I exhibit excellent inhibitory activity of one or more MMP enzymes, such as MMP-2, MMP-9 and MMP-13, while exhibiting substantially less inhibition of (at least) MMP-1. Also disclosed are metalloprotease inhibitor compds. having such selective activities, processes for manufacture of such compds., and pharmaceutical compns. using such inhibitors. The compds. are potentially useful against a wide variety of conditions, notably as antiinflammatory, antiangiogenesis, and antitumor agents. Over 900 example compds. are listed, most with supporting phys. data, and many with synthetic details. For instance, Et N-(tert-butoxycarbonyl)-4-(4-fluorophenylsulfonyl)-4-piperidinecarboxylate (preparation given) was subjected to a sequence of: (1) etherification with 4-(CF3S)C6H4OH (100%); (2) alkaline hydrolysis of the ester (100%); (3) amidation with THP-ONH2 (45%); and (4) acid deprotection of the THP ether (40%), to give title compound II.HCl. The latter salt selectively inhibited MMP-13 with IC50 0.2 nM, and MMP-2 with IC50 0.1 nM, but with IC50 >10,000 nM against MMP-1.

IT 308821-73-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of aromatic sulfone hydroxamic acids as metalloprotease inhibitors)

RN 308821-73-0 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[4-[[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]carbonyl]-1-piperidinyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

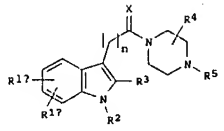


IT 35947-12-7, 1-(4-Methoxyphenyl)-2-methylpiperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of aromatic sulfone hydroxamic acids as metalloprotease inhibitors)

RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)





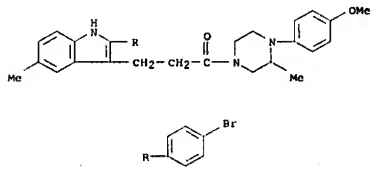


I

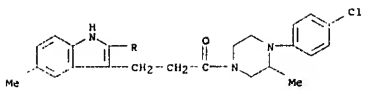
AB The title compds. [I; R1a, R1b = H, alkyl, alkoxy, etc.; R2 = H, alkyl, fluoroalkyl, etc.; R3 = (un)substituted Ph, biphenyl, naphthyl; R4 = H, alkyl, O (to form carbonyl), etc.; R5 = alkyl, cycloalkyl, cycloalkylalkyl, etc.; X = O, S; n = 1-4] and their pharmaceutically acceptable salts which are potent receptor antagonists of tachykinins, especially of the neurokinin-1 (substance P) receptor (no data), and useful in the treatment or prevention of depression, anxiety, pain, inflammation, migraine, emesis or postherpetic neuralgia, were prepared E.g., a synthesis of the piperazine I [R1a = 5-Me; R1b = H; R2 = H; R3 = 4-BrC6H4; R4 = H; R5 = 2-MeOC6H4; X = O; n = 2] was given. Compds. I are effective at 0.05-10 mg/kg/day in the treatment of conditions associated with an excess of tachykinins.

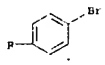
IT 290830-78-3P 290830-83-0P 290831-26-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-[(2-arylindol-3-yl)-1-oxoalkyl]piperazines as antagonists of tachykinins)

RN 290830-78-3 CAPLUS
CN Piperazine, 4-[3-[2-(4-bromophenyl)-5-methyl-1H-indol-3-yl]-1-oxopropyl]-1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)

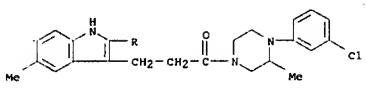


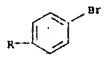
RN 290830-83-0 CAPLUS
CN Piperazine, 4-[3-[2-(4-bromophenyl)-5-methyl-1H-indol-3-yl]-1-oxopropyl]-1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)





RN 290831-26-4 CAPLUS
CN Piperazine, 4-[3-[2-(4-bromophenyl)-5-methyl-1H-indol-3-yl]-1-oxopropyl]-1-(3-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)





REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 23 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:608722 CAPLUS
DOCUMENT NUMBER: 133:193079
TITLE: Preparation of arylsulfonylheterocyclylhydroxamic acids and related compounds as matrix metalloprotease inhibitors
INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Boehm, Terri L.; Carroll, Jeffery N.; De Crescenzo, Gary A.; Fobian, Yvette M.; Freskos, John N.; Getman, Daniel P.; McDonald, Joseph J.; Hanson, Gunnar J.; Hockerman, Susan L.; Howard, Susan C.; Kolodziej, Steve A.; Li, Hui; Mischke, Deborah A.; Rico, Joseph G.; Stehle, Nathan W.; Tollefson, Michael B.; Vernier, William F.; Villamil, Clara I.; Rao, Shashidahar N.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 851 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

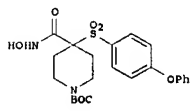




| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000050396 | A1 | 20000831 | WO 2000-US2518 | 20000222 <-- |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2001039287 | A1 | 20011108 | US 1999-256948 | 19990224 <-- |
| CA 2371876 | A1 | 20000831 | CA 2000-2371876 | 20000222 <-- |
| AU 200034785 | A | 20000914 | AU 2000-34785 | 20000222 <-- |
| HU 200200239 | A2 | 20020629 | HU 2002-239 | 20000222 <-- |
| EP 1230219 | A1 | 20020814 | EP 2000-913317 | 20000222 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| BR 2000008491 | A | 20020917 | BR 2000-8491 | 20000222 <-- |
| JP 2002537378 | T | 20021105 | JP 2000-600979 | 20000222 <-- |
| NZ 513648 | A | 20040227 | NZ 2000-513648 | 20000222 |
| NO 2001003963 | A | 20011023 | NO 2001-3963 | 20010815 <-- |
| ZA 2001006780 | A | 20020816 | ZA 2001-6780 | 20010816 <-- |
| IN 2001CN01174 | A | 20050304 | IN 2001-CN1174 | 20010821 |
| MX 2001PA08568 | A | 20020408 | MX 2001-PA8568 | 20010823 <-- |
| US 20021177588 | A1 | 20021128 | US 2001-954451 | 20010917 <-- |
| US 6750233 | B2 | 20040615 | | |

PRIORITY APPLN. INFO.:
US 1999-256948 A 19990224
US 1997-66007P P 19971114
US 1998-95347P P 19980804
US 1998-95501P P 19980806
US 1998-101080P P 19980918
WO 2000-US2518 W 20000222

OTHER SOURCE(S): MARPAT 133:193079
GI



I

AB A process for treating conditions associated with pathol. matrix metalloproteinase (MMP) activity comprises administration of compds. having inhibitory activity against >1 of MMP-2, MMP-9, and MMP-13, while exhibiting substantially less inhibition of MMP-1. The compds. are of the form HONHCOCR1R2SO2R3 [R1, R2 = H; R1R2 = atoms to form a 5-8 membered ring containing 1-3 heteroatoms; R3 = (substituted) aryl, heteroaryl]. Thus, 4-PhOC6H4SH was heated in Me2SO to give the disulfide dimer, which in THF was added to a mixture of Et N-tert-butoxycarbonylisonipecotate (preparation given) and LDA in THF at -60° to room temperature to give 40% sulfide, which was oxidized with m-ClC6H4CO(OOH) to give 59% sulfone. The Et ester was saponified with NaOH in EtOH/H2O to give 100% acid, which in DMF was

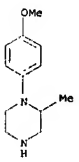




treated with hydroxybenzotriazole, EDC, 4-methylmorpholine, and aqueous NH2OH to give title compound I. I inhibited MMP-2 with IC50 = 0.2 nM. Pharmacol., pharmacokinetic, and toxicol. data are given for selected compds.

IT 35947-12-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of arylsulfonylheterocyclylhydroxamic acids and related compds. as matrix metalloprotease inhibitors)

RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 24 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:513446 CAPLUS
DOCUMENT NUMBER: 133:129863
TITLE: Heterocyclic compound modulators of the CCR5 receptor, preparation thereof, and therapeutic use
INVENTOR(S): Bondinell, William E.; Neeb, Michael J.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000042852 | A1 | 20000727 | WO 2000-US1908 | 20000125 <-- |
| W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1146790 | A1 | 20011024 | EP 2000-909984 | 20000125 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002535256 | T | 20021022 | JP 2000-594326 | 20000125 <-- |

PRIORITY APPLN. INFO.:
US 1999-117044P P 19990125
WO 2000-US1908 W 20000125

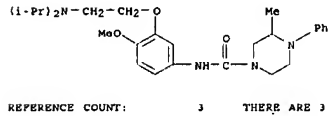




OTHER SOURCE(S): MARPAT 133:129863
AB Substituted heterocyclic compds. are provided which are modulators, agonists or antagonists of the CCR5 receptor. Also disclosed is the treatment and prevention of disease states mediated by CCR5, including, but no limited to, asthma and atopic disorders (for example, atopic dermatitis and allergies), rheumatoid arthritis, sarcoidosis and other fibrotic diseases, atherosclerosis, psoriasis, autoimmune diseases such as multiple sclerosis, and inflammatory bowel disease, all in mammals, by the use of substituted heterocyclic compds. which are CCR5 receptor antagonists. Furthermore, since CD8+ T cells have been implicated in COPD, CCR5 may play a role in their recruitment and therefore antagonists to CCR5 could provide potential therapeutic in the treatment of COPD. Also, since CCR5 is a co-receptor for the entry of HIV into cells, selective receptor modulators may be useful in the treatment of HIV infection.

IT 286387-94-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heterocyclic compound modulators of CCR5 receptor, preparation, and therapeutic use)

RN 286387-94-8 CAPLUS
CN 1-Piperazinecarboxamide, N-[3-[2-[bis(1-methylethyl)amino]ethoxy]-4-methoxyphenyl]-3-methyl-4-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 25 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:388555 CAPLUS
DOCUMENT NUMBER: 133:17747
TITLE: Preparation of 6-O-substituted erythromycins as antibacterial agents
INVENTOR(S): Or, Yat Sun; Clark, Richard F.; Ma, Zhenkun; Griesgraber, George; Li, Leping; Chu, Daniel T.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: U.S., 128 pp., Cont.-in-part of U.S. Ser. No. 646,477, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 6075011 | A | 20000613 | US 1997-841038 | 19970429 <-- |
| CA 2253330 | A1 | 19971113 | CA 1997-2253330 | 19970506 <-- |
| CA 2253330 | C | 20060725 | | |
| WO 9742206 | A1 | 19971113 | WO 1997-US7702 | 19970506 <-- |

W: AU, BR, CA, CN, CZ, HU, IL, JP, KR, MX, NZ
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

| | | | | | |
|---|---|---|---|---|---|
| AU 9729987 | A | 19971126 | AU 1997-29987 | 19970506 | <-- |
| AU 726075 | B2 | 20001026 | | | |
| ZA 9703894 | A | 19980223 | ZA 1997-3894 | 19970506 | <-- |
| CN 1224427 | A | 19990728 | CN 1997-196134 | 19970506 | <-- |
| BR 9708929 | A | 19990803 | BR 1997-8929 | 19970506 | <-- |
| HU 9902893 | A2 | 19991228 | HU 1999-2893 | 19970506 | <-- |
| HU 9902893 | A3 | 20000428 | | | |
| EP 1007530 | A1 | 20000614 | EP 1997-924605 | 19970506 | <-- |
| EP 1007530 | B1 | 20051116 | | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI

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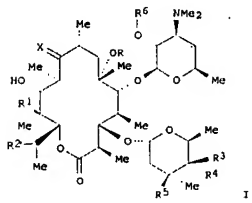
|---|---|---|---|---|---|
| NZ 332320 | A | 20000728 | NZ 1997-332320 | 19970506 | <-- |
| AT 310010 | T | 20051215 | AT 1997-924605 | 19970506 | |
| ES 2252784 | T3 | 20060516 | ES 1997-924605 | 19970506 | |
| KR 2000010800 | A | 20000225 | KR 1998-708934 | 19981106 | <-- |
| PRIORITY APPLN. INFO.: | | | US 1996-646477 | B2 19960507 | |
| | | | US 1997-841038 | A 19970429 | |
| | | | WO 1997-US7702 | W 19970506 | |

OTHER SOURCE(S): MARPAT 133:17747
GI



I

AB Macrolide erythromycins I (R = Me substituted with CN, F, carboxylate, sulfonate, amide, aryl, heteroaryl, substituted alkyl, alkenyl, alkynyl ;X = O, NOH, substituted oxime; R1 = H, OH; R2 = H, OH, halogen, amine, cycloalkyl, alkyl, aryl , OCONH-aryl, OCONH-heteroaryl; R3R4 = O, NOH, substituted oxime; R5 = OMe, F, OH; R6 = H, hydroxy protecting group) were prepared as antibacterial agents. Thus, I (R = allyl, R1 = R4 = OH, R2 = R3 = R6 = H, R5 = Me, X = O) was prepared and tested in vitro for its antibacterial activity (MIC = 0.01 to >100).

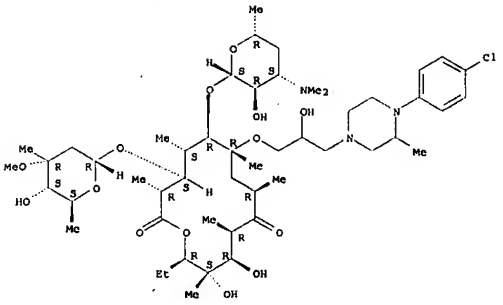
IT 198556-20-6P 198556-43-3P 198556-75-1P
198556-78-4P 198556-87-5P 271783-56-3P
271783-59-6P 271783-68-7P 273212-77-4P
273212-80-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 6-O-substituted erythromycins as antibacterial agents)





RN 198556-20-6 CAPLUS
CN Erythromycin, 6-O-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



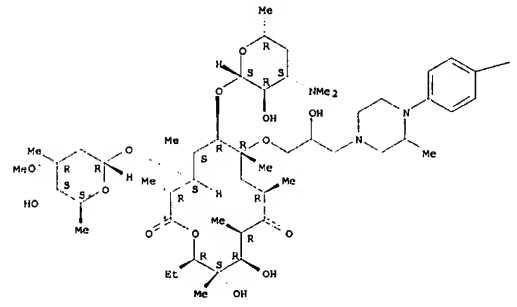
RN 198556-43-3 CAPLUS
CN Erythromycin, 6-O-[2-hydroxy-3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





PAGE 1-A



PAGE 1-B

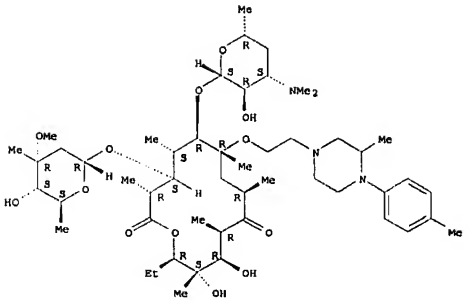
—OMe

RN 198556-75-1 CAPLUS
CN Erythromycin, 6-O-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

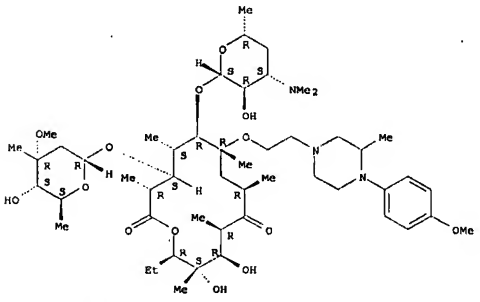






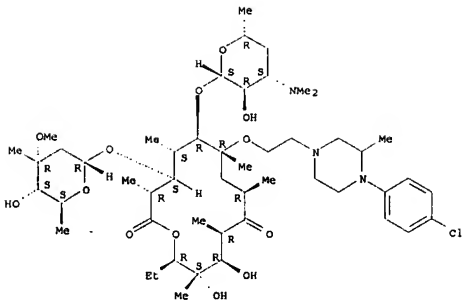
RN 198556-78-4 CAPLUS
CN Erythromycin, 6-O-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



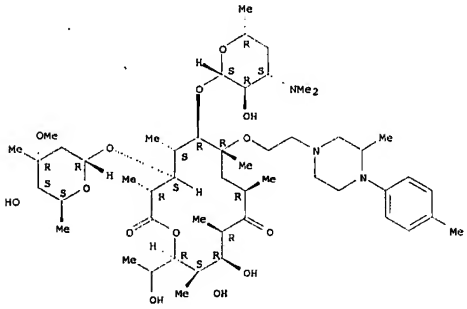
RN 198556-87-5 CAPLUS
CN Erythromycin, 6-O-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 271783-56-3 CAPLUS
CN Erythromycin, 14-hydroxy-6-O-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

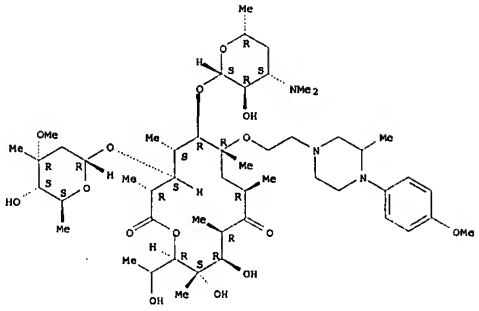


RN 271783-59-6 CAPLUS
CN Erythromycin, 14-hydroxy-6-O-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



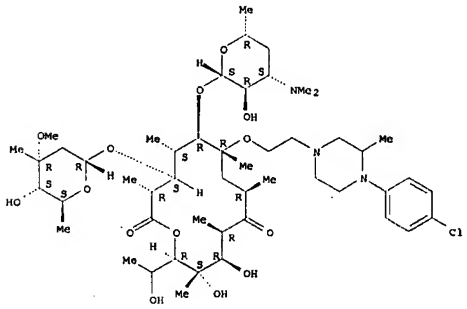


Absolute stereochemistry.



RN 271783-68-7 CAPLUS
CN Erythromycin, 6-O-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-14-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

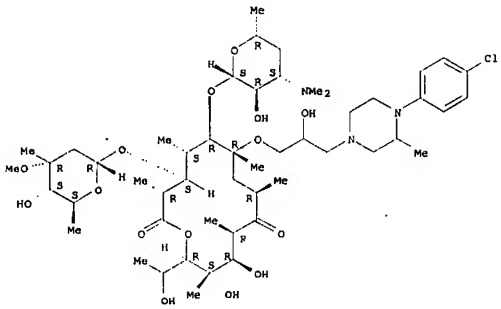






RN 273212-77-4 CAPLUS
CN Erythromycin, 6-O-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropyl]-14-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



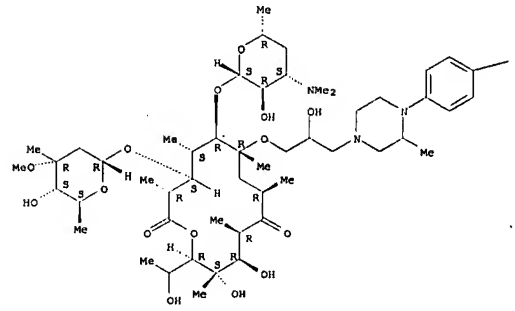
RN 273212-80-9 CAPLUS
CN Erythromycin, 14-hydroxy-6-O-[2-hydroxy-3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





PAGE 1-A



PAGE 1-B

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REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 26 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:241135 CAPLUS
DOCUMENT NUMBER: 132:279106
TITLE: Non-peptide GnRH agents, methods and intermediates for their preparation
INVENTOR(S): Anderson, Mark Brian; Vazir, Haresh N.; Luthin, David Robert; Paderes, Genevieve Deguzman; Pathak, Ved P.; Christie, Lance Christopher; Hong, Yufeng; Tompkins, Eileen Valenzuela; Li, Haitao; Faust, James
PATENT ASSIGNEE(S): Agouron Pharmaceuticals, Inc., USA; et al.
SOURCE: PCT Int. Appl., 444 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

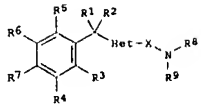
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| WO 2000020358 | A2 | 20000413 | WO 1999-US18790 | 19990820 | <-- |
| WO 2000020358 | A3 | 20001116 | | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | | |
| CA 2341346 | A1 | 20000413 | CA 1999-2341346 | 19990820 | <-- |
| BR 9913374 | A | 20010515 | BR 1999-13374 | 19990820 | <-- |
| EP 1105120 | A2 | 20010613 | EP 1999-968010 | 19990820 | <-- |
| EP 1105120 | B1 | 20050323 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | | |
| HU 200103622 | A2 | 20020429 | HU 2001-3622 | 19990820 | <-- |
| EE 200100102 | A | 20020617 | EE 2001-102 | 19990820 | <-- |
| SI 20746 | A | 20020630 | SI 1999-20076 | 19990820 | <-- |
| TR 200100631 | T2 | 20020821 | TR 2001-200100631 | 19990820 | <-- |
| JP 2002535244 | T | 20021022 | JP 2000-574479 | 19990820 | <-- |
| AU 759310 | B2 | 20030410 | AU 2000-24709 | 19990820 | |
| NZ 509252 | A | 20040528 | NZ 1999-509252 | 19990820 | |
| AT 291423 | T | 20050415 | AT 1999-968010 | 19990820 | |
| ES 2237966 | T3 | 20050801 | ES 1999-968010 | 19990820 | |
| NO 20010309 | A | 20010411 | NO 2001-309 | 20010119 | <-- |
| IN 2001DN00066 | A | 20070112 | IN 2001-DN66 | 20010124 | |
| ZA 2001000831 | A | 20020822 | ZA 2001-831 | 20010130 | <-- |
| MX 2001PA01834 | A | 20000821 | MX 2001-PA1834 | 20010219 | <-- |
| US 7101878 | B1 | 20060905 | US 2001-763216 | 20010220 | |
| LV 12732 | B | 20020320 | LV 2001-45 | 20010316 | <-- |
| BG 105362 | A | 20011231 | BG 2001-105362 | 20010319 | <-- |
| LT 4904 | B | 20020425 | LT 2001-24 | 20010319 | <-- |
| US 2004010033 | A1 | 20040115 | US 2003-353160 | 20030708 | |
| PRIORITY APPLN. INFO.: | | | US 1998-97520P | P 19980820 | |
| | | | WO 1999-US18790 | W 19990820 | |
| | | | US 2001-763216 | B3 20010220 | |

OTHER SOURCE(S): MARPAT 132:279106
GI







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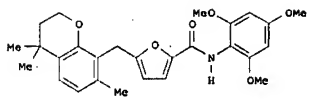


II

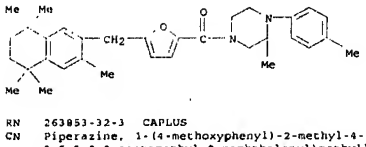
AB Non-peptide GnRH agents capable of inhibiting the effect of gonadotropin-releasing hormone are described. The compds. and their pharmaceutically acceptable salts, multimers, prodrugs, and active metabolites are suitable for treating mammalian reproductive disorders and steroid hormone-dependent tumors as well as for regulating fertility, where suppression of gonadotropin release is indicated. The compds. include those of formula I [X = C:O, C:S, S:O, or SO2; Het = 5-membered NOS-heterocycle; R1, R2 = H, alkyl; R3-R7 = H, halo, (un)substituted alkyl, aryl, heteroaryl, CH2OR, OR, CO2R; R = alkyl, aryl, etc.; adjacent rings positions such as R6R7 may form (un)substituted 5- or 6-membered ring with up to 4 heteroatoms; R8 = lipophilic moiety such as alkyl, aryl, CH2OR, OR, etc.; R9 = H, (un)substituted alkyl]. Methods and intermediates for synthesizing the compds. are also described. For instance, 4,4,7-trimethylchroman (preparation given) was alkylated in the 6- and 8-positions using Et 5-(chloromethyl)-2-furoate (46% total yield), and the resulting esters were hydrolyzed to a mixture of acids. This unsepd. mixture was treated with SOCl2 and amidated with 2,4,6-trimethoxyphenylamine-HCl to give the invention compound II and its chroman-6-position isomer, which were separated by HPLC. Several compds. exhibited high affinity (<100 nM) at human GnRH receptors. The compds. antagonized GnRH-stimulated inositol phosphate accumulation in cells with recombinant human GnRH receptors, and an example compound reduced plasma LH levels in castrated male rats. Various biol. data for several hundred compds. are given.

IT 263853-05-0P 263853-32-3P 263855-06-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of non-peptide GnRH agents for regulating gonadotropin secretion)

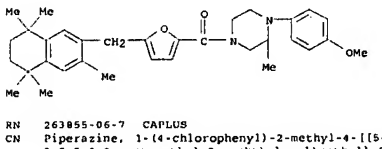
RN 263853-05-0 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)-4-[[5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-2-furanyl]carbonyl]- (9CI) (CA INDEX NAME)



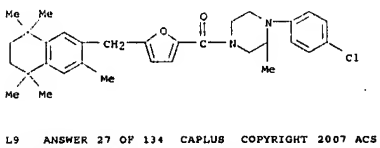




RN 263853-32-3 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl-4-[[5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-2-furanyl]carbonyl]- (9CI) (CA INDEX NAME)



RN 263855-06-7 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl-4-[[5-[(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)methyl]-2-furanyl]carbonyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 27 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2000:210118 CAPLUS |
| DOCUMENT NUMBER: | 132:237107 |
| TITLE: | Preparation of piperazino-substituted cyanophenyl derivatives as antiandrogen agents |
| INVENTOR(S): | Taniguchi, Nobuaki; Kinoyama, Isao; Kamikubo, Takashi; Toyoshima, Akira; Samizu, Kiyohiro; Kawaminami, Eiji; Imamura, Masakazu; Moritomo, Hiroyuki; Matsuhisa, Akira; Hirano, Masaaki; Miyazaki, Yoji; Nozawa, Eisuke; Okada, Minoru; Koutoku, Hiroshi; Ohta, Mitsuaki |
| PATENT ASSIGNEE(S): | Yamanouchi Pharmaceutical Co., Ltd., Japan; et al. |
| SOURCE: | PCT Int. Appl., 65 pp.<br>CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | Japanese |
| FAMILY ACC. NUM. COUNT: | 1 |
| PATENT INFORMATION: | |





| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000017163 | A1 | 20000330 | WO 1999-JP5149 | 19990921 <-- |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2345146 | A1 | 20000330 | CA 1999-2345146 | 19990921 <-- |
| AU 9956544 | A1 | 20000410 | AU 1999-56544 | 19990921 <-- |
| AU 754529 | B2 | 20021121 | | |
| BR 9914018 | A | 20010703 | BR 1999-14018 | 19990921 <-- |
| EP 1122242 | A1 | 20010808 | EP 1999-943446 | 19990921 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 3390744 | B2 | 20030331 | JP 2000-574073 | 19990921 |
| JP 2003137873 | A | 20030514 | JP 2002-328498 | 19990921 |
| CN 1129581 | B | 20031203 | CN 1999-811198 | 19990921 |
| RU 2221785 | C2 | 20040120 | RU 2001-107612 | 19990921 |
| US 6673799 | B1 | 20040106 | US 2001-787672 | 20010321 |
| US 2004010037 | A1 | 20040115 | US 2003-608341 | 20030630 |
| PRIORITY APPLN. INFO.: | | | JP 1998-267508 | A 19980922 |
| | | | JP 1999-155398 | A 19990602 |
| | | | JP 2000-574073 | A3 19990921 |
| | | | WO 1999-JP5149 | W 19990921 |
| | | | US 2001-787672 | A3 20010321 |

OTHER SOURCE(S): MARPAT 132:237107
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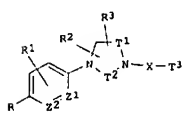
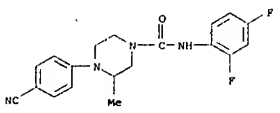


I

AB The title compds. I [T1 = (CH2)n; T2 = (CH2)k; T3 = (NR4Y)mR5; R = cyano, etc.; R1 = H, halo, etc.; R2 - R4 = H, alkyl, etc.; R5 = alkyl, etc.; k, n = 1 - 3; m = 0 or 1; X = CO, etc.; Z1, Z2 = CH, N; a proviso is given; Y = alkylene, etc.] are prepared These derivs. exhibit antiandrogen activities and are therefore useful in the prevention or treatment of prostatic cancer, prostatic hypertrophy and so forth. In an in vitro assay for inhibition of androgen binding to androgen receptors, (2R,5S)-N-(2-bromo-4-pyridyl)-4-(4-cyano-3-trifluoromethylphenyl)-2,5-dimethylpiperazine-1-carboxamide showed the Ki value of 7.5 nM.

IT 262294-07-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazino-substituted cyanophenyl derivs. as antiandrogen.

agents)
RN 262294-07-5 CAPLUS
CN 1-Piperazinecarboxamide, 4-(4-cyanophenyl)-N-(2,4-difluorophenyl)-3-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 28 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:190924 CAPLUS
DOCUMENT NUMBER: 132:237088
TITLE: Preparation of fused pyridine inhibitors of cGMP phosphodiesterase
INVENTOR(S): Macor, John E.; Yu, Guixue
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000015222 | A1 | 20000323 | WO 1999-US21070 | 19990913 <-- |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6326379 | B1 | 20011204 | US 1999-393833 | 19990910 <-- |
| CA 2342583 | A1 | 20000323 | CA 1999-2342583 | 19990913 <-- |
| AU 9961438 | A1 | 20000403 | AU 1999-61438 | 19990913 <-- |
| AU 751486 | B2 | 20020815 | | |
| EP 1113796 | A1 | 20010711 | EP 1999-948211 | 19990913 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |

PRIORITY APPLN. INFO.: US 1998-100665P P 19980916
WO 1999-US21070 W 19990913
OTHER SOURCE(S): MARPAT 132:237088
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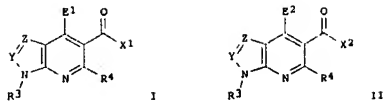
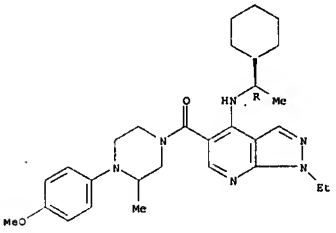


I II

AB The title compds. [I or II; E1 = OR1, SR1, NH-A1-cycloalkyl, etc.; E2 = NH-A1-alkoxy, NH-A1-CO2alkyl, NH-A1-aryl, etc.; R1 = A1-cycloalkyl, A1-alkoxy, A1-aryl, etc.; X1 = OA1R2, OR9, NR9R10, etc.; X2 = OA1R25, N(R5)A2R25, etc.; X3 = OR9, OA1OR9, NR9R10, etc.; A1 = (un)substituted alkylene; Y = N, CR6; Z = N, CR7 with the proviso that at least one of Y and Z = N; R3 = H, alkyl, cycloalkyl, etc.; R6, R7 = H, alkyl, cycloalkyl, etc.; R4 = H, 1- or 3-imidazolyl, etc.; A2 = a direct bond, alkylene, alkenyl, etc.; R2 = cycloalkyl, aryl, heteroaryl, etc.; R25 = cycloalkyl, aryl, heteroaryl, etc.; R5 = H, alkyl, cycloalkyl, etc.; R9, R10 = H, alkyl, cycloalkyl, etc.], useful for treating a cGMP PDE (especially type V) associated condition such as erectile dysfunction, were prepared Thus, reacting 4-[[(3-chloro-4-methoxyphenyl)methyl]amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid with 4-aminomethylpyridine in the presence of EDAC.HCl, 1-hydroxybenzotriazole and Et3N in THF afforded 90% II [Y = N; Z = CH; E2 = 3-Cl-4-MeOC6H3CH2NH; X2 = 4-pyridynylmethylamino; R3 = Et; R4 = H]. Compds. I are effective at 0.05-100 mg/kg/day.
IT 261770-09-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused pyridine inhibitors of cGMP phosphodiesterase)
RN 261770-09-6 CAPLUS
CN Piperazine, 4-[[4-[[(1R)-1-cyclohexylethyl]amino]-1-ethyl-1H-pyrazolo[3,4-b]pyridin-5-yl]carbonyl]-1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.







REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 29 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:691093 CAPLUS
DOCUMENT NUMBER: 131:310284
TITLE: Preparation of substituted diamines as α4β1 mediated cell adhesion inhibitors
INVENTOR(S): Mccarthy, Clive; Harris, Neil Victor; Morley, Andrew David
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Limited, UK
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9954321 | A1 | 19991028 | WO 1999-GB1230 | 19990421 <-- |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9937164 | A | 19991108 | AU 1999-37164 | 19990421 <-- |

PRIORITY APPLN. INFO.: GB 1998-8431 A 19980421
GB 1998-11417 A 19980528
US 1998-104139P P 19981014
US 1998-104238P P 19981014
WO 1999-GB1230 W 19990421
OTHER SOURCE(S): MARPAT 131:310284
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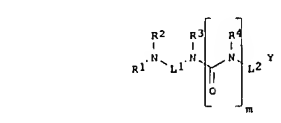

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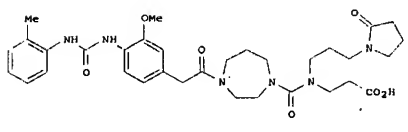
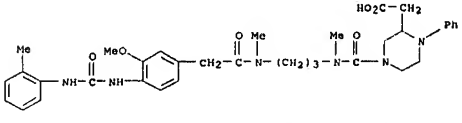


II





AB Substituted diamines (I) (wherein R1 = lower alkyl or various combinations of substituents, such as (cyclo)alkyl, (cyclo)alkenyl, (cyclo)alkynyl, (hetero)aryl(alkyl), etc., and linkage groups, such as C(O), C(S), (un)substituted NHC(O) or NHC(S), S(O), SO2, heteroaryldiyl, heterocycloalkylene, phenylene, etc.; R2 = H or lower alkyl; R3 and R4 = independently H or (un)substituted alkyl, alkenyl, or alkynyl; or R3 and R4 together may = (CH2)n or C(O)CH:CH; L1 = alkylene or (un)substituted (CHR10)pAr(CHR10)p; or L1N(R3) = (un)substituted alkylheterocyclo; or N(R2)L1 = (un)substituted heterocycloalkyl; or N(R2)L1N(R3) = diaza heterocyclo; L2 = (un)substituted alkylene, alkenylene, alkynylene, cycloalkenylene, cycloalkylene, or heterocycloalkylene; Y = carboxy (or an acid bioisostere) or (un)substituted C(O)NH2; Ar = phenylene, (hetero)cycloalkylene, or heteroaryldiyl; R10 = H or lower alkyl; m = 0 or 1; n = 2-4; p = 0-3] were prepd by solid phase synthesis as α4β1 mediated cell adhesion inhibitors. For example, the ureido derivative (II) was prepared using a Wang resin support. The resin was loaded with acryloyl chloride and treated sequentially with 1-(3-aminopropyl)-2-pyrrolidinone, triphosgene, homopiperazine, and 3-methoxy-4-[3-(2-methylphenyl)ureido]phenylacetic acid to yield II. Compds. of formula I regulate the interaction of VCAM-1 and fibronectin with the integrin VLA-4 (α4β1). Particular compds. of the invention suppressed cell adhesion to fibronectin and VCAM-1 with IC50 values ranging from 100μM to 1 nM in assays on metabolically labeled RAMOS cells. Particular compds. also inhibited airway inflammation after antigen challenge in mice and rats. The inhibitors caused a statistically significant reduction in eosinophil and lymphocyte nos. in bronchoalveolar lavage (BAL) and airway tissue. The invention compds., their prodrugs, pharmaceutically acceptable salts, and solvates, are useful for the treatment of inflammatory diseases and asthma.
IT 247253-69-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of substituted diamines as α4β1 mediated cell adhesion inhibitors for treatment of inflammatory diseases and asthma)
RN 247253-69-6 CAPLUS
CN 2-Piperazineacetic acid, 4-[[[3-[[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]methylamino]propyl]methylamino]carbonyl]-1-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 30 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:350651 CAPLUS

DOCUMENT NUMBER: 131:18929
TITLE: Preparation of arylsulfonylheterocyclylhydroxamic acids and related compounds as matrix metalloprotease inhibitors
INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Boehm, Terri L.; De Crescenzo, Gary A.; Villamil, Clara I.; McDonald, Joseph J.; Freskos, John N.; Getman, Daniel P.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 840 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

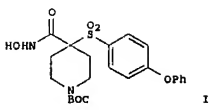
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9925687 | A1 | 19990527 | WO 1998-US23242 | 19981112 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2306460 | A1 | 19990527 | CA 1998-2306460 | 19981112 <-- |
| AU 9913732 | A | 19990607 | AU 1999-13732 | 19981112 <-- |
| AU 756150 | B2 | 20030102 | | |
| BR 9814643 | A | 20001003 | BR 1998-14643 | 19981112 <-- |
| EP 1042290 | A1 | 20001011 | EP 1998-957485 | 19981112 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| JP 2001523662 | T | 20011127 | JP 2000-521071 | 19981112 <-- |
| NZ 503485 | A | 20021025 | NZ 1998-503485 | 19981112 <-- |
| RU 2250105 | C2 | 20050420 | RU 2000-115948 | 19981112 |
| ZA 9810412 | A | 19991209 | ZA 1998-10412 | 19981113 <-- |
| US 2001014688 | A1 | 20010816 | US 1998-191129 | 19981113 <-- |
| NO 2000002469 | A | 20000712 | NO 2000-2469 | 20000512 <-- |
| MX 2000PA04660 | A | 20010930 | MX 2000-PA4660 | 20000512 <-- |
| US 6541489 | B1 | 20030401 | US 2000-554082 | 20000731 |
| US 2002177588 | A1 | 20021128 | US 2001-954451 | 20010917 <-- |
| US 6750233 | B2 | 20040615 | | |
| US 2004048852 | A1 | 20040311 | US 2003-337942 | 20030107 |
| US 6890937 | B2 | 20050510 | | |
| US 2006084688 | A1 | 20060420 | US 2005-46645 | 20050128 |

PRIORITY APPLN. INFO.: US 1997-66007P P 19971114
US 1998-95347P P 19980804
US 1998-95501P P 19980806
US 1998-101080P P 19980918
WO 1998-US23242 W 19981112
US 1999-256948 B3 19990224
US 2000-554082 A3 20000731
US 2003-337942 A3 20030107

OTHER SOURCE(S): MARPAT 131:18929
GI







I

AB A process for treating conditions associated with pathol. matrix metalloproteinase (MMP) activity comprises administration of compds. having inhibitory activity against >1 of MMP-2, MMP-9, and MMP-13, while exhibiting substantially less inhibition of MMP-1. The compds. are of the form HONHCOCR1R2SO2R3 [R1, R2 = H; R1R2 = atoms to form a 5-8 membered ring containing 1-3 heteroatoms; R3 = (substituted) aryl, heteroaryl]. Thus, 4-PhOC6H4SH was heated in Me2SO to give the disulfide dimer, which in THF was added to a mixture of Et N-tert-butoxycarbonylisonipecotate (preparation given) and LDA in THF at -60° to room temperature to give 405 sulfide, which was oxidized with m-ClC6H4CO(OOH) to give 59% sulfone. The Et ester was saponified with NaOH in EtOH/H2O to give 100% acid, which in DMF was treated with hydroxybenzotriazole, EDC, 4-methylmorpholine, and aqueous NH2OH to give title compound (I). I inhibited MMP-2 with IC50 = 0.2 nM.
1T 35947-12-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of arylsulfonylheterocyclylhydroxamic acids and related compds. as matrix metalloprotease inhibitors)
RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 31 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:297413 CAPLUS
DOCUMENT NUMBER: 130:311821
TITLE: Preparation of 1-[(isoindolyl- and isoquinolylamino)alkyl]-4-arylpiperazines and analogs as dopamine D4 receptor ligands
INVENTOR(S): He, Xiao-shu; De Costa, Brian; Wasley, Jan W. F.
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2



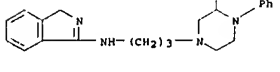


DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9921848 | A2 | 19990506 | WO 1998-US22665 | 19981026 <-- |
| WO 9921848 | A3 | 19990715 | | |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9911223 | A | 19990517 | AU 1999-11223 | 19981026 <-- |

PRIORITY APPLN. INFO.: US 1997-958694 A 19971027
WO 1998-US22665 W 19981026

OTHER SOURCE(S): MARPAT 130:311821
AB Title compds., e.g, R1NR6Z1Z2(CH2)mR [I; R = (un)substituted (hetero)aryl; R1 = (un)substituted 1-isoindolyl, -1-isoquinolyl, etc.; R6 = H or alkyl; Z1 = alkylene; Z2 = piperidine- or piperazine-1,4-diyl; m = 0-2] were prepared Thus, 1-chloroisoquinoline was aminated by 4-(5-fluoro-2-pyrimidinyl)-1-pyrazineethylamine (preparation given) to give I (R = 5-fluoro-2-pyrimidinyl, R1 = 1-isoquinolyl, R6 = H, Z1 = CH2CH2, Z2 = piperazine-1,4-diyl). Data for biol. activity of I were given.
IT 186345-30-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study; unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-[(isoindolyl- and isoquinolylamino)alkyl]-4-arylpiperazines and analogs as dopamine D4 receptor ligands)
RN 186345-30-2 CAPLUS
CN 1H-Isoindol-3-amine, N-[3-(3-methyl-4-phenyl-1-piperazinyl)propyl)-, dihydrobromide. (9CI) (CA INDEX NAME)



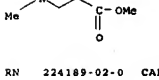
●2 HBr

L9 ANSWER 32 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:235769 CAPLUS
DOCUMENT NUMBER: 130:338083
TITLE: Hybridized and isosteric analogs of N1-acetyl-N4-dimethylpiperazinium iodide (ADMP) and N1-phenyl-N4-dimethylpiperazinium iodide (DMPP) with central nicotinic action

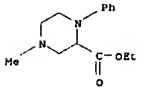




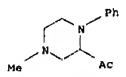
AUTHOR(S): Manetti, Dina; Bartolini, Alessandro; Borea, Pier Andrea; Bellucci, Cristina; Dei, Silvia; Ghelardini, Carla; Gualtieri, Fulvio; Romanelli, Maria Novella; Scapecchi, Serena; Teodori, Elisabetta; Varani, Katia
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Firenze, Florence, 50121, Italy
SOURCE: Bioorganic & Medicinal Chemistry (1999), 7(3), 457-465
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of piperazine derivs., obtained by hybridization of N1-acetyl-N4-dimethylpiperazinium iodide (ADMP) and N1-phenyl-N4-dimethylpiperazinium iodide (DMPP) or of the corresponding tertiary bases with arecoline and arecolone or by isosteric substitution of the Ph ring of DMPP, has been synthesized. Hybridization afforded compds. that, both as tertiary bases and as iodomethylates, have no affinity for the nicotinic receptor. On the contrary, isosteric substitution gave compds. that maintain affinity for the receptor; among them, 1-methyl-4-(3- or 4-pyridinyl)piperazine show affinity in the nanomolar range for the nicotinic receptor. The pharmacol. profile of these isomeric compds. is quite interesting as they present differences in their peripheral and central effects, suggesting that they interact with different subtypes of the nicotinic receptor.
IT 224189-00-8P 224189-02-0P 224189-13-3P 224189-15-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(hybridized and isosteric analogs of N1-acetyl- and N1-phenyl-N4-dimethylpiperazinium iodide with central nicotinic action)
RN 224189-00-8 CAPLUS
CN 2-Piperazinecarboxylic acid, 4-methyl-1-phenyl-, methyl ester (9CI) (CA INDEX NAME)



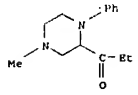
RN 224189-02-0 CAPLUS
CN 2-Piperazinecarboxylic acid, 4-methyl-1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



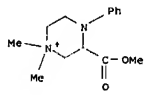
RN 224189-13-3 CAPLUS
CN Ethanone, 1-(4-methyl-1-phenyl-2-piperazinyl)- (9CI) (CA INDEX NAME)



RN 224189-15-5 CAPLUS
CN 1-Propanone, 1-(4-methyl-1-phenyl-2-piperazinyl)- (9CI) (CA INDEX NAME)



IT 224189-01-9P 224189-03-1P 224189-14-4P
224189-16-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(hybridized and isosteric analogs of N1-acetyl- and N1-phenyl-N4-dimethylpiperazinium iodide with central nicotinic action)
RN 224189-01-9 CAPLUS
CN Piperazinium, 3-(methoxycarbonyl)-1,1-dimethyl-4-phenyl-, iodide (9CI) (CA INDEX NAME)

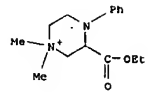


● I⁻

RN 224189-03-1 CAPLUS
CN Piperazinium, 3-(ethoxycarbonyl)-1,1-dimethyl-4-phenyl-, iodide (9CI) (CA INDEX NAME)

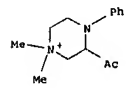






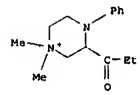
● I⁻

RN 224189-14-4 CAPLUS
CN Piperazinium, 3-acetyl-1,1-dimethyl-4-phenyl-, iodide (9CI) (CA INDEX NAME)



● I⁻

RN 224189-16-6 CAPLUS
CN Piperazinium, 1,1-dimethyl-3-(1-oxopropyl)-4-phenyl-, iodide (9CI) (CA INDEX NAME)



● I⁻

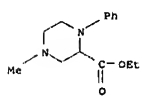
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 33 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:234565 CAPLUS
DOCUMENT NUMBER: 131:18981
TITLE: Design and Synthesis of Imidazoline Derivatives Active on Glucose Homeostasis in a Rat Model of Type II Diabetes. 2. Syntheses and Biological Activities of 1,4-Dialkyl-, 1,4-Dibenzyl, and 1-Benzyl-4-alkyl-2-(4',5'-dihydro-1'H-imidazol-2'-yl)piperazines and





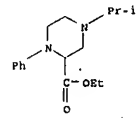
Isosteric Analogs of Imidazoline
AUTHOR(S): Le Bihan, Gaeelle; Rondu, Frederic; Pele-Tounian, Agnes; Wang, Xuan; Lidy, Sandrine; Touboul, Estera; Lamouri, Aazdine; Dive, Georges; Huet, Jack; Pfeiffer, Bruno; Renard, Pierre; Guardiola-Lemaitre, Beatrice; Manechez, Dominique; Penicaud, Luc; Ktorza, Alain; Godfroid, Jean-Jacques
CORPORATE SOURCE: Laboratoire de Pharmacochimie Moleculaire et Systemes Membranaires, Universite Paris 7-Denis Diderot, Paris, 75251, Fr.
SOURCE: Journal of Medicinal Chemistry (1999), 42(9), 1587-1603
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Piperazine deriva. were identified as new antidiabetic compds. Structure-activity relationship studies in a series of 1-benzyl-4-alkyl-2-(4',5'-dihydro-1'H-imidazol-2'-yl)piperazines resulted in the identification of 1-methyl-4-(2',4'-dichlorobenzyl)-2-(4',5'-dihydro-1'H-imidazol-2'-yl)piperazine, PMS 812 (S-21663), as a highly potent antidiabetic agent on a rat model of diabetes, mediated by an important increase of insulin secretion independently of α2-adrenoceptor blockage. These studies were extended to find addnl. compds. in these series with improved properties. In such a way, substitution of both piperazine N atoms was first optimized by using various alkyl, branched or not, and benzyl groups. Second, some modifications of the imidazoline ring and its replacement by isosteric heterocycles were carried out, proceeding from PMS 812, to evaluate their influence on the antidiabetic activity. The importance of the distance between the imidazoline ring and the piperazine skeleton was studied third. Finally, the influence of the N-benzyl moiety was also analyzed compared to a direct N-Ph substitution. The pharmacol. evaluation was performed in vivo using glucose tolerance tests on a rat model of type II diabetes. The most active compds. were 1,4-diisopropyl-2-(4',5'-dihydro-1'H-imidazol-2'-yl)piperazine, PMS 847 (S-22068), and 1,4-diisobutyl-2-(4',5'-dihydro-1'H-imidazol-2'-yl)piperazine, PMS 889 (S-22575), which strongly improved glucose tolerance without any side event or hypoglycemic effect. More particularly, PMS 847 proved to be as potent after po (100 μmol/kg) as after i.p. administration and appears as a good candidate for clin. investigations.
IT 224189-02-0P 226068-23-1P 226068-29-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antidiabetic activity of and (benzyl)(alkyl)(imidazolyl)piperazines and isosteric analogs)
RN 224189-02-0 CAPLUS
CN 2-Piperazinecarboxylic acid, 4-methyl-1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



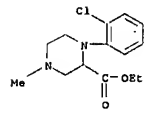




RN 226068-23-1 CAPLUS
CN 2-Piperazinecarboxylic acid, 4-(1-methylethyl)-1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)

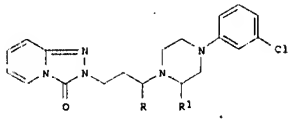


RN 226068-29-7 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-(2-chlorophenyl)-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 34 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:89740 CAPLUS
DOCUMENT NUMBER: 130:209646
TITLE: Effect of Modifications of the Alkylpiperazine Moiety of Trazodone on 5HT2A and σ1 Receptor Binding Affinity
AUTHOR(S): Giannangeli, Marilena; Cazzolla, Nicola; Luparini, Maria Rita; Magnani, Maurizio; Mabilia, Massimo; Picconi, Giuseppe; Tomaselli, Mauro; Baiocchi, Leandro
CORPORATE SOURCE: Department of Medicinal Chemistry, Angelini Ricerche S.p.A., S. Palomba-Pomezia, 00040, Italy
SOURCE: Journal of Medicinal Chemistry (1999), 42(1), 336-345
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



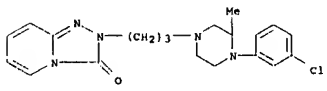
I

AB A series of triazolopyridine derivs. were synthesized in order to explore the effect of modifications of the alkylpiperazine moiety of trazodone on binding affinity for 5HT2A and α1 receptors. All of the synthesized compds. show a decrease of affinity for both 5HT2A and α1 receptors, as compared to trazodone, with the exception of I [R = Me, R1 = H; R = H, R1 = Me]. These compds. showed a decrease of affinity only for the α1 receptor. The stereochem. influence of the piperazine moiety of I [R = H, R1 = Me] was also evaluated. Enantiomer (S)-I [R = H, R1 = Me] showed the most significant differences between 5HT2A and α1 receptor affinity (IC50 values) and among the corresponding functional properties (pA2 values). Since (S)-I [R = H, R1 = Me] cannot generate the metabolite 4-(3-chlorophenyl)piperazine this product was selected for further pharmacol. studies.

IT 151448-02-1P 220909-95-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(effect of modifications of the alkylpiperazine moiety of Trazodone on 5HT2A and α1 receptor binding affinity)

RN 151448-02-1 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyridin-3(2H)-one, 2-[3-[4-(3-chlorophenyl)-3-methyl-1-piperazinyl]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 220909-95-5 CAPLUS

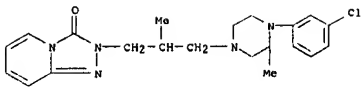
CN 1,2,4-Triazolo[4,3-a]pyridin-3(2H)-one, 2-[3-[4-(3-chlorophenyl)-3-methyl-1-piperazinyl]-2-methylpropyl]-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 220909-94-4
CMF C21 H26 Cl N5 O



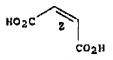




CM 2

CRN 110-16-7
CMF C4 H4 O4

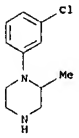
Double bond geometry as shown.



IT 75348-33-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(effect of modifications of the alkylpiperazine moiety of Trazodone on 5HT2A and α1 receptor binding affinity)

RN 75348-33-3 CAPLUS

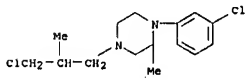
CN Piperazine, 1-(3-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



IT 220909-98-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(effect of modifications of the alkylpiperazine moiety of Trazodone on 5HT2A and α1 receptor binding affinity)

RN 220909-98-8 CAPLUS

CN Piperazine, 4-(3-chloro-2-methylpropyl)-1-(3-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



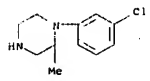




IT 220910-03-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(effect of modifications of the alkylpiperazine moiety of Trazodone on 5HT2A and α1 receptor binding affinity)

RN 220910-03-2 CAPLUS

CN Piperazine, 1-(3-chlorophenyl)-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 35 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:34895 CAPLUS

DOCUMENT NUMBER: 130:95566

TITLE: Preparation of tropone derivatives for remedies/preventives for frequent urination/urinary incontinence

INVENTOR(S): Koga, Ichiro; Narita, Kazuhisa; Okada, Atsushi

PATENT ASSIGNEE(S): Nippon Kayaku Kabushiki Kaisha, Japan

SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

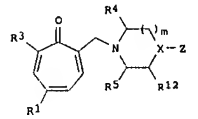
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| WO 9900366 | A1 | 19990107 | WO 1998-JP2865 | 19980626 | <-- |
| W: AU, CA, CN, JP, KR, US | | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | | |
| CA 2294312 | A1 | 19990107 | CA 1998-2294312 | 19980626 | <-- |
| AU 9879341 | A | 19990119 | AU 1998-79341 | 19980626 | <-- |
| AU 736510 | B2 | 20010726 | | | |
| EP 995741 | A1 | 20000426 | EP 1998-929705 | 19980626 | <-- |
| R: AT, CH, DE, FR, GB, IT, LI, SE | | | | | |
| US 6221868 | B1 | 20010424 | US 1999-446423 | 19991220 | <-- |
| PRIORITY APPLN. INFO.: | | | JP 1997-186030 | A 19970627 | |
| | | | JP 1997-225552 | A 19970808 | |
| | | | JP 1997-256223 | A 19970905 | |
| | | | WO 1998-JP2865 | W 19980626 | |

OTHER SOURCE(S): MARPAT 130:95566

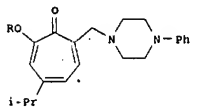
GI







I



II

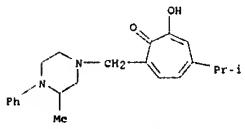
AB Claimed are remedies/preventives for frequent urination/urinary incontinence which contain as the active ingredient compds. having a tropone skeleton or pharmacol. acceptable salts thereof and novel compds. having the tropone skeleton. The compds. having a tropone skeleton and showing the above pharmacol. effects are those represented by, for example, general formula [I; R1, R2 = hydrogen, (un)substituted lower alkyl or aryl; R3 = OR6 or NR7R8; wherein R6 = H, (un)substituted lower alkyl, aralkyl, or acyl; R7, R8 = H, optionally heteroatom-substituted lower alkyl, (un)substituted aralkyl; or R7 and R8 together represent a 5- to 10-membered ring optionally containing O or NR9; wherein R9 = H, (un)substituted lower alkyl or aryl; R4 , R5 = H, lower alkyl; R12 = H, lower alkyl; X = N, CH; Z = CH(Ar1)(Ar2), (un)substituted Ph, CH2Ph, benzoyl, 2-pyridyl, or 2-pyrimidinyl; Ar1, Ar2 = (un)substituted aryl; m = 1,2]. These compds. increase bladder volume and prolong urination intervals by inhibiting urination reflex, does not exhibit the side effects of anticholinergic agents such as dry mouth and ischuria (retention of urine), and are effective for patients in whom increase in atropine-resistant contraction are noticed. Thus, 37% aqueous formalin solution was added to a solution of 8.2 g hinokitiol, 7.8 mL 1-phenylpiperazine, and 2.9 mL AcOH in 5 mL MeOH and heated at 60° fro 2.5 h to give 7-(4-phenylpiperazinomethyl)-2,4,6-cycloheptatrien-1-one derivative (II; R = H), which was ethylated by di-Et sulfate in the presence of K2CO3 in acetone under reflux for 6 h to give II (R = Et). II (R = H) and II (R = Et) at 5 mg/kg i.v. prolonged the ratio of interval of rat rhythmic bladder contraction before and after the administration of the compds. by the factor of 12.7 and 22.3, resp.

IT 219145-21-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tropone derivs. for remedies/preventives for frequent urination/urinary incontinence)

RN 219145-21-8 CAPLUS

CN 2,4,6-Cycloheptatrien-1-one, 2-hydroxy-4-(1-methylethyl)-7-[(3-methyl-4-

phenyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



IT 2946-76-1P, 2-Methyl-1-phenylpiperazine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of tropone derivs. for remedies/preventives for frequent urination/urinary incontinence)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 36 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:604657 CAPLUS
DOCUMENT NUMBER: 129:245169
TITLE: Preparation of 1,4-disubstituted piperazines as alpha 1a adrenergic receptor antagonists
INVENTOR(S): Bock, Marg G.; Patane, Michael A.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 18 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5807856 | A | 19980915 | US 1996-747687 | 19961112 <-- |
| PRIORITY APPLN. INFO.: | | | US 1996-747687 | 19961112 |
| OTHER SOURCE(S): | MARPAT 129:245169 | | | |

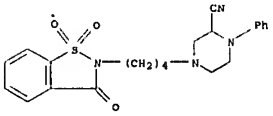
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *





AB The title compds. [I or II; W = (un)substituted Ph, pyridyl, thienyl, etc.; R1, R2 = CN, CONR4R5, CO2R4, SO2R4; R3 = III; R4, R5 = H, C1-8 alkyl, C3-8 cycloalkyl; R7 = C1-8 alkyl, iso-Pr, (un)substituted Ph, etc.; T, U, X, Y, Z = H, halo, C1-8 alkyl, etc.; n = 2-6], useful as selective alpha 1a adrenergic receptor antagonists in treating benign prostatic hyperplasia, were prepared Thus, reaction of piperazine IV.HCl with amide V in the presence of iPr2NEt in DMF afforded the title compound VI. Representative compds. I and II showed Ki of ≤300 nM against alpha 1a adrenergic receptor binding. Compds. I and II are selective in their ability to relax smooth muscle tissue enriched in the alpha 1a receptor subtype without at the same time inducing orthostatic hypotension. One such tissue is found surrounding the urethral lining. Therefore, one utility of the instant compds. is to provide acute relief to males suffering from benign prostatic hyperplasia, by permitting less hindered urine flow. Another utility of the instant compds. is provided by combination with a human 5-alpha reductase inhibitory compound, such that both acute and chronic relief from the effects of benign prostatic hyperplasia are achieved.
IT 191156-62-4P 191156-63-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1,4-disubstituted piperazines as alpha 1a adrenergic receptor antagonists)
RN 191156-62-4 CAPLUS
CN 2-Piperazinecarbonitrile, 4-[4-(1,1-dioxido-3-oxo-1,2-benzisothiazol-2(3H)-yl)butyl]-1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

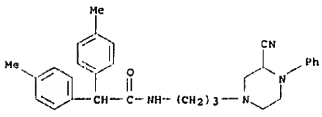


● HCl

RN 191156-63-5 CAPLUS
CN Benzeneacetamide, N-[3-(3-cyano-4-phenyl-1-piperazinyl)propyl]-4-methyl-α-(4-methylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)

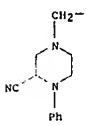






● HCl

IT 135036-22-5P 191156-64-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1,4-disubstituted piperazines as alpha 1a adrenergic receptor antagonists)
RN 135036-22-5 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 191156-64-6 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

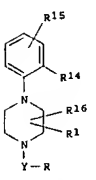
● HCl

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 37 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:352630 CAPLUS
DOCUMENT NUMBER: 129:27960
TITLE: Preparation of piperazine derivatives as tocolytic oxytocin receptor antagonists
INVENTOR(S): Bock, Mark G.; Evans, Ben E.; Culberson, J. Christopher; Gilbert, Kevin F.; Rittle, Kenneth E.; Williams, Peter D.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 37 pp., Cont.-in-part of U.S. 5,464,788.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

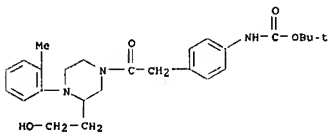
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5756504 | A | 19980526 | US 1996-718415 | 19960923 <-- |
| US 5464788 | A | 19951107 | US 1994-217270 | 19940324 <-- |
| WO 9525443 | A1 | 19950928 | WO 1995-US3738 | 19950323 <-- |
| W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, US, UZ | | | | |
| RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: | | | US 1994-217270 | A2 19940324 |
| | | | WO 1995-US3738 | W 19950323 |
| OTHER SOURCE(S): | MARPAT 129:27960 | | | |

GI

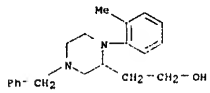


AB The title compds. I [Y = SO2, (CH2)p,CO(CH2)p, etc.; p = 1-3; R = (un)substituted Ph, etc.; R1 = H, cyano, Ph, CONHR2, CONR2R2, etc.; R2 = H, C3-8 cycloalkyl or C1-5 alkyl; R14, R15 = C1-5 alkyl or alkoxy, halo; R16 = H or oxo] were prepared I are useful as oxytocin and vasopressin receptor antagonists. Thus, spiro[1H]indene-1,4'-piperidine.HCl was treated with 2,4-dimethoxy-phenylacetic acid in the presence of EDC, HBT and Et3N to give 1'-(2,4-dimethoxyphenylacetyl)-spiro[1H]indene-1,4'-piperidine, which showed IC50 of 400 nM for [3H]oxytocin.
IT 170929-79-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine derivs. as tocolytic oxytocin receptor

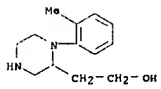
antagonists)
RN 170929-79-0 CAPLUS
CN Carbamic acid, [4-[2-[3-(2-hydroxyethyl)-4-(2-methylphenyl)-1-piperazinyl]-2-oxoethyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT 170930-08-2P 170930-09-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazine derivs. as tocolytic oxytocin receptor antagonists)
RN 170930-08-2 CAPLUS
CN 2-Piperazineethanol, 1-(2-methylphenyl)-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 170930-09-3 CAPLUS
CN 2-Piperazineethanol, 1-(2-methylphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 38 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:55616 CAPLUS
DOCUMENT NUMBER: 128:114961
TITLE: Preparation of tetrahydrobenzindole derivatives for the treatment or prevention of mental diseases
INVENTOR(S): Koyama, Masao; Kikuchi, Chika; Ushiroda, Osamu; Ando, Takashi; Nagaso, Hiroshi; Fuji, Kazuyuki; Okuno,



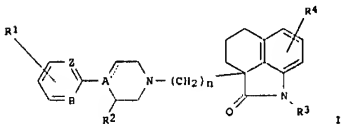


Masayo; Hiranuma, Toyokazu
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9800400 | A1 | 19980108 | WO 1997-JP2226 | 19970627 <-- |
| W: CA, JP, NO, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2259218 | A1 | 19980108 | CA 1997-2259218 | 19970627 <-- |
| CA 2259218 | C | 20060725 | | |
| EP 937715 | A1 | 19990825 | EP 1997-928490 | 19970627 <-- |
| EP 937715 | B1 | 20050601 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| AT 296801 | T | 20050615 | AT 1997-928490 | 19970627 |
| ES 2243999 | T3 | 20051201 | ES 1997-928490 | 19970627 |
| NO 9806141 | A | 19990217 | NO 1998-6141 | 19981228 <-- |
| NO 311515 | B1 | 20011203 | | |
| US 6355642 | B1 | 20020312 | US 1998-214114 | 19981228 <-- |

PRIORITY APPLN. INFO.:
JP 1996-169702 A 19960628
JP 1997-96271 A 19970415
JP 1997-130201 A 19970521
JP 1997-144376 A 19970603
WO 1997-JP2226 W 19970627

OTHER SOURCE(S): MARPAT 128:114961
GI

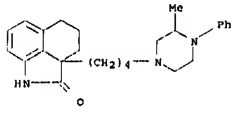


AB The title compds. I [A represents N, CH, C having a double bond or CR5; B and Z independently represent each N, CH or CR1, provided that A is N when B and/or Z is N; R1 represents hydrogen, halogeno, lower alkyl, cyano, trihalomethyl, hydroxy, alkoxy, alkylthio, alkylsulfenyl, alkylsulfonyl, alkoxycarbonyl, sulfamoyl, optionally substituted amino, optionally alkylated carbamoyl, acyl or carboxy; R2 represents hydrogen or lower alkyl; R3 represents hydrogen, lower alkyl; R3 represents hydrogen, lower alkyl or aralkyl; R4 represents hydrogen, halogeno, lower alkyl, hydroxyl, alkoxy, acyl, alkoxycarbonyl, nitro, optionally substituted amino, optionally alkylated carbamoyl or acyloxy; R5 represents lower alkyl, cyano, carbamoyl, carboxy, acyl, acyloxy, alkoxy, alkoxycarbonyl,



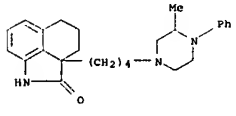


trihalomethyl or hydroxy; and n is an integer of from 2 to 6] are prepared 1 strongly inhibit [3H]-serotonin and [3H]-5-CT binding to the human serotonin 5-HT7 receptor subtype expressed in a cultured cell line and are useful for treating or preventing mental diseases. 2A-[4-[4-(2-Methoxyphenyl)piperazinyl]butyl]-2a,3,4,5-tetrahydrobenz[cd]indol-2-(1H)-one was prepared from 2a,3,4,5-tetrahydrobenz[cd]indol-2-(1H)-one. In tests for affinity for the 5-HT7 receptors, compds. of this invention showed Ki values of 8.9 nM to 27 nM. The title compds. showed selective affinity for 5-HT7 receptors.
IT 201608-75-5P 201608-76-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tetrahydrobenzindole derivs. for treatment or prevention of mental diseases)
RN 201608-75-5 CAPLUS
CN Benz[cd]indol-2(1H)-one, 2a,3,4,5-tetrahydro-2a-[4-(3-methyl-4-phenyl-1-piperazinyl)butyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

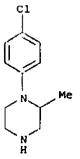
RN 201608-76-6 CAPLUS
CN Benz[cd]indol-2(1H)-one, 2a,3,4,5-tetrahydro-2a-[4-(3-methyl-4-phenyl-1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)



IT 55117-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of tetrahydrobenzindole derivs. for treatment or prevention of mental diseases)
RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)

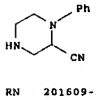




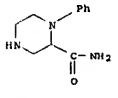


IT 2946-76-1P 201609-32-7P 201609-33-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of tetrahydrobenzindole derivs. for treatment or prevention of mental diseases)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 201609-32-7 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl- (9CI) (CA INDEX NAME)



RN 201609-33-8 CAPLUS
CN 2-Piperazinecarboxamide, 1-phenyl- (9CI) (CA INDEX NAME)



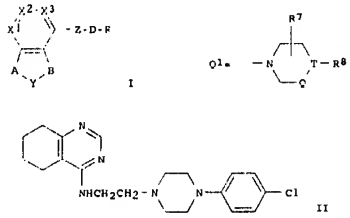
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 39 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:13943 CAPLUS

DOCUMENT NUMBER: 128:61522
TITLE: Preparation of fused heterocyclic compounds as antagonists of D2 and D4 receptors
INVENTOR(S): Kuroita, Takanobu; Togo, Yoshifumi; Ishibuchi, Seigo; Fujio, Masakazu; Futamura, Takashi
PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9747601 | A1 | 19971218 | WO 1997-JP1993 | 19970609 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9729807 | A | 19980107 | AU 1997-29807 | 19970609 <-- |
| JP 3531169 | B2 | 20040524 | JP 1998-501435 | 19970609 |
| PRIORITY APPLN. INFO.: | | | JP 1996-149620 A | 19960611 |
| | | | WO 1997-JP1993 W | 19970609 |

OTHER SOURCE(S): MARPAT 128:61522
GI



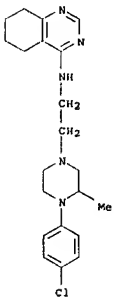
AB Fused heterocyclic compds. represented by general formula (I; X1-X2-X3 = NCR1N, CR1CR2N, NCR1CR2, CR1NCR2, NNCR1; R1, R2 = H, alkyl, OH, NH2, arylalkyl, (un)substituted aryl or heteroaryl; A = linear or branched and (un)substituted C1-4 alkyl; Y = O, S, SO, SO2, (un)substituted NH; B = linear or branched alkyl and (un)substituted C1-4 alkylene; Z = O, S, SO, SO2, (un)substituted NH, CH(OH), CO, CH2; D = linear or branched alkyl





C1-8 alkylene; R = heterocyclyl, e.g., Q1; wherein Q-T = (CH2)n, CH2CH, CH:C; wherein R7 = H, alkyl; R8 = (un)substituted aromatic hydrocarbyl or heterocyclyl) or optical isomers or pharmaceutically acceptable salts thereof are prepared Also claimed are medicinal compns. comprising these compds. and pharmaceutically acceptable additives, and drugs comprising these compds. These compds. exert more potent blocking effects on D4 receptors than on D2 receptors. Moreover, they have high affinities for receptors other than dopamine receptors such as muscarine M1, and serotonin-2 (5-HT2) and adrenalin α1 and α2 receptors. Thus, these compds. are efficacious against not only pos. symptoms typified by hallucination and delusion characteristic of the acute stage of schizophrenia but also neg. symptoms such as emotional torpidity, abulia, and autism. In addition, they are useful as antipsychotic agents with relieved side effects such as extrapyramidal symptoms and abnormal internal secretion observed in association with the administration of the conventional antipsychotic agents having only D2 receptor antagonism. The above compds. are usable as remedies for diseases such as schizophrenia. Thus, N-(5,6,7,8-tetrahydroquinazolin-4-yl)-2-chloroacetamide (preparation given) and N-(4-chlorophenyl)piperazine hydrochloride were dissolved in DMF and stirred with K2CO3 and KI at room temperature for 24 h to give N-(5,6,7,8-tetrahydroquinazolin-4-yl)-2-[4-(4-chlorophenyl)piperazin-1-yl]acetamide, which was reduced by LiAlH4 in THF at room temperature for 30 min to give the title compound (II). II and another compound tested in vitro showed affinity for D2 and D4 receptors of nerve synapses membrane with Ki value of 25 nM and 0.01-1 nM, resp.

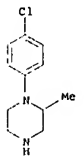
IT 200412-33-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused heterocyclic compds. having antagonism for D2 and D4 receptors as antipsychotics)
RN 200412-33-5 CAPLUS
CN 4-Quinazolinamine, N-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



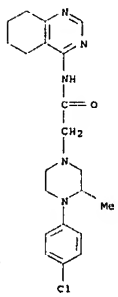




IT 55117-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of fused heterocyclic compds. having antagonism for D2 and D4 receptors as antipsychotics)
RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



IT 200413-37-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of fused heterocyclic compds. having antagonism for D2 and D4 receptors as antipsychotics)
RN 200413-37-2 CAPLUS
CN 1-Piperazineacetamide, 4-(4-chlorophenyl)-3-methyl-N-(5,6,7,8-tetrahydro-4-quinazolinyl)- (9CI) (CA INDEX NAME)



L9 ANSWER 40 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:746060 CAPLUS

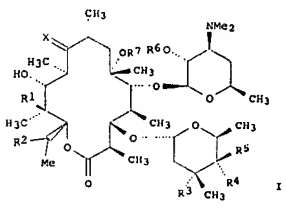




DOCUMENT NUMBER: 127:359051
TITLE: Preparation of 6-O-substituted erythromycins as bactericides
INVENTOR(S): Or, Yat Sun; Clark, Richard F.; Ma, Zhenkun; Griesgraber, George; Li, Laping; Chu, Daniel T.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 225 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9742206 | A1 | 19971113 | WO 1997-US7702 | 19970506 <-- |
| W: AU, BR, CA, CN, CZ, HU, IL, JP, KR, MX, NZ | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 6075011 | A | 20000613 | US 1997-841038 | 19970429 <-- |
| CA 2253330 | A1 | 19971113 | CA 1997-2253330 | 19970506 <-- |
| CA 2253330 | C | 20060725 | | |
| AU 9729987 | A | 19971126 | AU 1997-29987 | 19970506 <-- |
| AU 726075 | B2 | 20001026 | | |
| BR 9708929 | A | 19990803 | BR 1997-8929 | 19970506 <-- |
| EP 1007530 | A1 | 20000614 | EP 1997-924605 | 19970506 <-- |
| EP 1007530 | B1 | 20051116 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| NZ 332320 | A | 20000728 | NZ 1997-332320 | 19970506 <-- |
| JP 2002515034 | T | 20020521 | JP 1997-540164 | 19970506 |
| AT 310010 | T | 20051215 | AT 1997-924605 | 19970506 |
| PRIORITY APPLN. INFO.: | | | US 1996-646477 A | 19960507 |
| | | | US 1997-841038 A | 19970429 |
| | | | WO 1997-US7702 W | 19970506 |

OTHER SOURCE(S): MARPAT 127:359051
GI



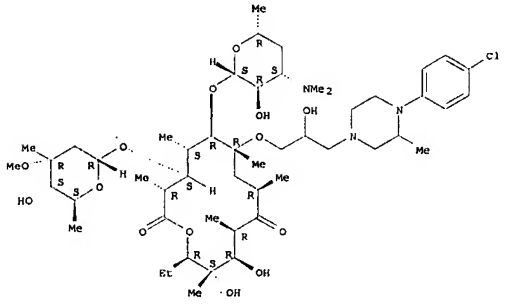
AB Antimicrobial erythromycins, e.g. I (X = O, NOH, NOR; R = alkyl, aralkyl, cycloalkyl, arylsilyl; R1, R2 = H, OH; R3 = OMe, F, OH; R4, R5 = one is H and the other is OH, alkyl, aralkyl, sulfone; R4, R5 = X; R6 = H, hydroxy protecting group; R7 = F, alkyl, alkenyl, alkynyl sulfone, amide), were

prepared as bactericides. Thus, I (X = O; R1 = R4= OH; R2 = R5 = R6 = H; R3 = OMe, R7 = Pr) was prepared and tested for its in vitro antibacterial activity (MIC = 0.05-100).

IT 198556-20-6P 198556-43-3P 198556-75-1P
198556-78-4P 198556-87-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of 6-O-substituted erythromycins as bactericides)

RN 198556-20-6 CAPLUS
CN Erythromycin, 6-O-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



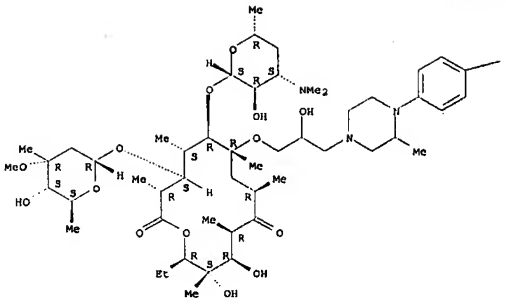
RN 198556-43-3 CAPLUS
CN Erythromycin, 6-O-[2-hydroxy-3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





PAGE 1-A



PAGE 1-B

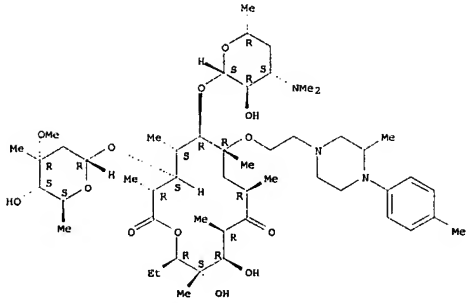
—OMe

RN 198556-75-1 CAPLUS
CN Erythromycin, 6-O-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

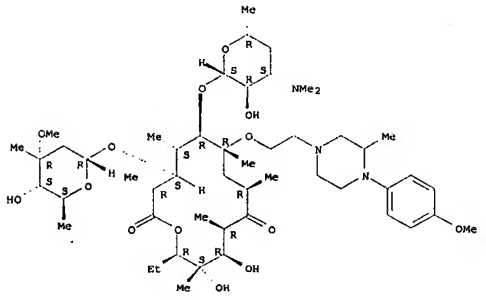






RN 198556-78-4 CAPLUS
CN Erythromycin, 6-O-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

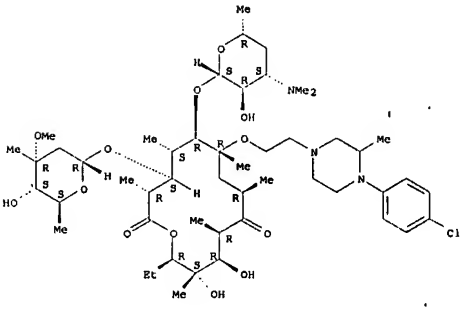


RN 198556-87-5 CAPLUS
CN Erythromycin, 6-O-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.







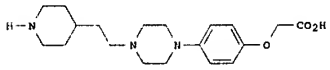
L9 ANSWER 41 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:684389 CAPLUS
DOCUMENT NUMBER: 127:358876
TITLE: Preparation of heterocyclylphenoxyalkanoates and analogs as cell aggregation inhibitors
INVENTOR(S): Pieper, Helmut; Linz, Gunter; Austel, Volkhard; Himmelsbach, Frank; Guth, Brian; Weisenberger, Johannes
PATENT ASSIGNEE(S): Dr. Karl Thomae G.m.b.H., Germany
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9737975 | A1 | 19971016 | WO 1997-EP1698 | 19970404 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| DE 19614204 | A1 | 19971016 | DE 1996-19614204 | 19960410 <-- |
| US 5994356 | A | 19991130 | US 1997-832259 | 19970403 <-- |
| CA 2244860 | A1 | 19971016 | CA 1997-2244860 | 19970404 <-- |
| AU 9726368 | A | 19971029 | AU 1997-26368 | 19970404 <-- |
| EP 892783 | A1 | 19990127 | EP 1997-918113 | 19970404 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | | |

IE, FI

| | | | | | | |
|---|---|---|---|---|---|---|
| JP 2000508307 | T | 20000704 | JP 1997-535832 | | 19970404 | <-- |
| ZA 9703002 | A | 19981009 | ZA 1997-3002 | | 19970409 | <-- |
| PRIORITY APPLN. INFO.: | | | DE 1996-19614204 | A | 19960410 | |
| | | | WO 1997-EP1698 | W | 19970404 | |

OTHER SOURCE(S): MARPAT 127:358876
GI

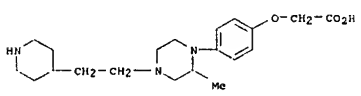


II

AB R1Z1Z2Z3Z4Z5R [I; R = OH, alkoxy, OPh, etc.; R1 = H, (phenyl)alkyl, etc.; Z1 = (oxo)piperazine-1,4-diyl, (oxo)piperidine-1,4-diyl; Z2 = CH2CH2, COCH2, NHCO, CO2, etc.; Z3 = (un)substituted (oxo)piperazine-1,4-diyl, -(oxo)piperidine-1,4- or 4,1-diyl, ,-cyclohexylene, etc.; Z4 = piperidinediyl, phenylene, cyclohexylene, etc.; Z5 = OCH2CO, NHCH2CO, CH2CO, etc.] were prepared Thus, Me 4-piperazinophenoxyacetate was N-alkylated by 2-(1-tert-butoxycarbonyl-4-piperidinyl)ethyl methanesulfonate and the product converted in 2 steps to give title compound II.2HCl. Data for biol. activity of I were given.

IT 198626-02-7P 198626-25-4P 198626-78-7P
198627-21-3P 198627-41-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclylphenoxyalkanoates and analogs as cell aggregation inhibitors)

RN 198626-02-7 CAPLUS
CN Acetic acid, [4-[2-methyl-4-[2-(4-piperidinyl)ethyl]-1-piperazinyl]phenoxy]-, dihydrochloride (9CI) (CA INDEX NAME)

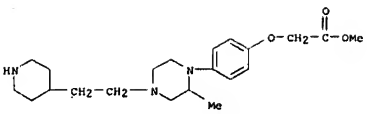


●2 HCl

RN 198626-25-4 CAPLUS
CN Acetic acid, [4-[2-methyl-4-[2-(4-piperidinyl)ethyl]-1-piperazinyl]phenoxy]-, methyl ester, dihydrochloride (9CI) (CA INDEX NAME)

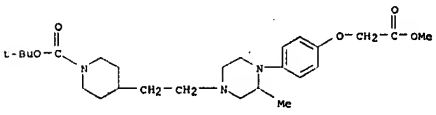




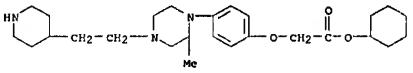


●2 HCl

RN 198626-78-7 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-[2-[4-[4-(2-methoxy-2-oxoethoxy)phenyl]-3-methyl-1-piperazinyl]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

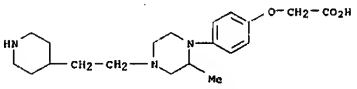


RN 198627-21-3 CAPLUS
CN Acetic acid, [4-[2-methyl-4-[2-(4-piperidinyl)ethyl]-1-piperazinyl]phenoxy]-, cyclohexyl ester, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 198627-41-7 CAPLUS
CN Acetic acid, [4-[2-methyl-4-[2-(4-piperidinyl)ethyl]-1-piperazinyl]phenoxy]- (9CI) (CA INDEX NAME)

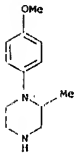






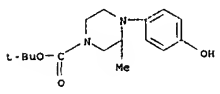
IT 35947-12-7, 1-(4-Methoxyphenyl)-2-methylpiperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclylphenoxyalkanoates and analogs as cell aggregation inhibitors)

RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)

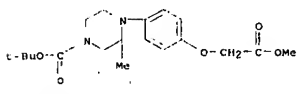


IT 198627-59-7P 198627-60-0P 198627-62-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclylphenoxyalkanoates and analogs as cell aggregation inhibitors)

RN 198627-59-7 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(4-hydroxyphenyl)-3-methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 198627-60-0 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-(2-methoxy-2-oxoethoxy)phenyl]-3-methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



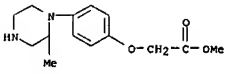
RN 198627-62-2 CAPLUS
CN Acetic acid, [4-(2-methyl-1-piperazinyl)phenoxy]-, methyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1





CRN 198627-61-1
CMF C14 H20 N2 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2

L9 ANSWER 42 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 1997:456780 CAPLUS |
| DOCUMENT NUMBER: | 127:50667 |
| TITLE: | Preparation of piperazine derivatives as alpha 1a adrenergic receptor antagonists |
| INVENTOR(S): | Bock, Mark G.; Patane, Michael A. |
| PATENT ASSIGNEE(S): | Merck and Co., Inc., USA; Bock, Mark G.; Patane, Michael A. |
| SOURCE: | PCT Int. Appl., 59 pp. CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | English |
| FAMILY ACC. NUM. COUNT: | 1 |
| PATENT INFORMATION: | |

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9718209 | A1 | 19970522 | WO 1996-US18346 | 19961112 <-- |
| W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9677344 | A | 19970605 | AU 1996-77344 | 19961112 <-- |
| PRIORITY APPLN. INFO.: | | | US 1995-7964P | P 19951115 |
| | | | GB 1996-5165 | A 19960312 |
| | | | WO 1996-US18346 | W 19961112 |

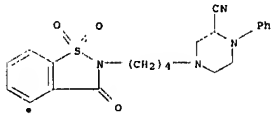
OTHER SOURCE(S): MARPAT 127:50667
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; W = (un)substituted Ph, pyridyl, thienyl, etc.; R1, R2 = H, CN, CHNR4R5, CO2R4, SO2R4 (wherein R4, R5 = H, C1-8 alkyl, C3-8 cycloalkyl); R3 = II, III (wherein R6 = H, Cl; R7 = C1-8 alkyl, etc.; T, U, X, Y, Z = H, halo, C1-8 alkyl, C3-8 cycloalkyl, etc.; n = 2-6)] and their salts, selective alpha 1a adrenergic receptor antagonists and useful in the treatment of benign prostatic hyperplasia, were prepared Thus, reaction of 2-cyano-1-phenylpiperazine with 4-bromobutylsaccharin in the presence of EtN(iPr)2 in DMF afforded IV.HCl which Ki of ≤ 300 nM against alpha 1a adrenergic receptor binding. Compds. I are selective in their ability to relax smooth muscle tissue enriched in the alpha 1a receptor subtype without at the same time inducing orthostatic hypotension. One such tissue is found surrounding the urethral lining. Therefore, one utility of the instant compds. is to provide acute relief to males suffering from benign prostatic hyperplasia, by permitting less hindered urine flow. Another utility of the instant compds. is provided by combination with a human 5-alpha reductase inhibitory compound, such that both acute and chronic relief from the effects of benign prostatic hyperplasia are achieved.

IT 191156-62-4P 191156-63-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine derivs. as alpha 1a adrenergic receptor antagonists)

RN 191156-62-4 CAPLUS
CN 2-Piperazinecarbonitrile, 4-[4-(1,1-dioxido-3-oxo-1,2-benzisothiazol-2(3H)-yl)butyl]-1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

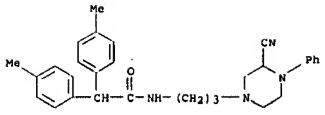


● HCl

RN 191156-63-5 CAPLUS
CN Benzeneacetamide, N-[3-(3-cyano-4-phenyl-1-piperazinyl)propyl]-4-methyl-α-(4-methylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



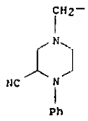




● HCl

IT 135036-22-5P 191156-64-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazine derivs. as alpha 1a adrenergic receptor antagonists)

RN 135036-22-5 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 191156-64-6 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

L9 ANSWER 43 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:443299 CAPLUS
DOCUMENT NUMBER: 127:65787
TITLE: Preparation of piperazine and piperidine derivatives as alpha 1a adrenergic receptor antagonists
INVENTOR(S): Bock, Mark G.; Patane, Michael A.; Ponticello, Rose Ann



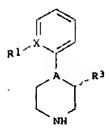


Ann
PATENT ASSIGNEE(S): Merck And Co., Inc., USA; Bock, Mark G.; Patane, Michael A.; Ponticello, Rose Ann
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9717967 | A1 | 19970522 | WO 1996-US18321 | 19961112 <-- |
| W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2235370 | A1 | 19970522 | CA 1996-2235370 | 19961112 <-- |
| AU 9677343 | A | 19970605 | AU 1996-77343 | 19961112 <-- |
| AU 710337 | B2 | 19990916 | | |
| EP 865280 | A1 | 19980923 | EP 1996-940465 | 19961112 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| JP 11507395 | T | 19990629 | JP 1996-519091 | 19961112 <-- |
| US 5922722 | A | 19990713 | US 1998-66477 | 19980422 <-- |

PRIORITY APPLN. INFO.: US 1995-6765P P 19951115
GB 1996-3423 A 19960219
WO 1996-US18321 W 19961112

OTHER SOURCE(S): MARPAT 127:65787
GI



I

AB I [A = CR2, N; X = C, N, but when X = N, R1 is absent; R1 = H, halo, alkyl, haloalkyl, alkoxy, cyano, CONR4R5, cycloalkyl; R2 = H, cyano, CONR4R5, CO2R4; R3 = H, cyano, CONR4R5, CO2R4, SO2R4; R4, R5 = H, alkyl, cycloalkyl were prepared as alpha 1a adrenergic receptor antagonists (no data). I may be used for treating benign prostatic hyperplasia (no data). E.g., reaction of (ClCH2CH2)2N(BOC) and 2-ClC6H4CH2CN in THF/DMF/NaH, followed by treatment of the piperidine product with HCl/HOAc gave 4-(2-chlorophenyl)-4-cyanopiperidine hydrochloride.

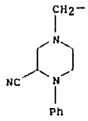
IT 135036-22-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU





(Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of piperazine and piperidine derivs. as alpha 1a adrenergic receptor antagonists)

RN 135036-22-5 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



IT 191156-64-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine and piperidine derivs. as alpha 1a adrenergic receptor antagonists)

RN 191156-64-6 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

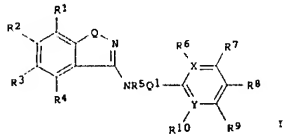
● HCl

L9 ANSWER 44 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:119141 CAPLUS
DOCUMENT NUMBER: 126:131469
TITLE: Preparation of 1-[N-(aralkylaminoalkyl)]aminoisoindoles as dopamine receptor ligands.
INVENTOR(S): He, Xiao-Shu; Decosta, Brian; Wasley, Jan W. F.
PATENT ASSIGNEE(S): Neurogen Corporation, USA; He, Xiao-Shu; Decosta, Brian; Wasley, Jan W. F.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| WO 9639403 | | A1 | 19961212 | WO 1996-US8836 | 19960604 <-- |
| W: | AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG | | | | |
| RW: | KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI | | | | |
| US 5602168 | | A | 19970211 | US 1995-464336 | 19950605 <-- |
| US 5656632 | | A | 19970812 | US 1995-463037 | 19950605 <-- |
| US 5744472 | | A | 19980428 | US 1995-463430 | 19950605 <-- |
| AU 9659826 | | A | 19961224 | AU 1996-59826 | 19960604 <-- |
| WO 9829410 | | A1 | 19980709 | WO 1997-US967 | 19970102 <-- |
| W: | AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, US, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: | KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9715820 | | A | 19980731 | AU 1997-15820 | 19970102 <-- |
| PRIORITY APPLN. INFO.: | | | | US 1995-463037 | A2 19950605 |
| | | | | US 1995-463430 | A2 19950605 |
| | | | | US 1995-464336 | A 19950710 |
| | | | | WO 1996-US8836 | W 19960604 |
| | | | | WO 1997-US967 | W 19970102 |

OTHER SOURCE(S): MARPAT 126:131469
GI



AB Title compds. (I; R1, R2, R3, R4, R7, R8, R9 = H, halo, OH, alkyl, alkoxy; X, Y, Z = C, N; R7R8 = atoms to form a (substituted) benzo ring; R6, R10 = H, halo, OH, alkyl, alkoxy, electron pair; R11 = R6, (substituted) Ph; R5 = H, alkyl; Q = (CH2)l; l = 1-4; Q1 = (CH2)mNR12CR14R15CR16R17ZR11R13(CH2)n; m = 2-5; n = 0-4; R12, R13 = alkyl; R12R13 = (CH2)s; s = 1-6; R14-R17 = H, alkyll, were prepared Thus, phthalimidine was stirred with Me3OBF4 to give a residue which was refluxed with 1-(3-aminopropyl)-4-(2-pyrimidinyl)piperazine and Et3N in CHCl3 to give 1-[3-[1-[4-(2-pyrimidinyl)piperazinyl]propyl]amino]isoindole. The latter bound to D4 receptors with Ki = 0.070 mM.

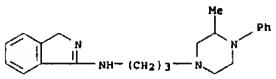
IT 186345-23-3P 186345-30-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-[N-(aralkylaminoalkyl)]aminoisoindoles as dopamine



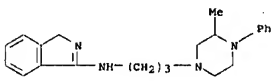


receptor ligands)

RN 186345-23-3 CAPLUS
CN 1H-Isoindol-3-amine, N-[3-(3-methyl-4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



RN 186345-30-2 CAPLUS
CN 1H-Isoindol-3-amine, N-[3-(3-methyl-4-phenyl-1-piperazinyl)propyl]-, dihydrobromide (9CI) (CA INDEX NAME)



●2 HBr

L9 ANSWER 45 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:628533 CAPLUS
DOCUMENT NUMBER: 125:275875
TITLE: Preparation of imidazo[1,2-a]pyridines dopamine D4-receptor antagonist cardiovascular and CNS agents
INVENTOR(S): Tenbrink, Ruth E.
PATENT ASSIGNEE(S): Pharmacia and Upjohn Company, USA
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

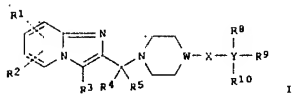
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9625414 | A1 | 19960822 | WO 1996-US1114 | 19960212 <-- |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD | | | | |
| AU 9648595 | A | 19960904 | AU 1996-48595 | 19960212 <-- |
| EP 809642 | A1 | 19971203 | EP 1996-904507 | 19960212 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | | |





| | | | | | |
|---|---|---|---|---|---|
| IE, SI, LT, LV | | | | | |
| JP 11500123 | T | 19990106 | JP 1996-524966 | 19960212 <-- |
| US 5912246 | A | 19990615 | US 1997-894179 | 19970814 <-- |
| US 6013654 | A | 20000111 | US 1998-222560 | 19981230 <-- |
| PRIORITY APPLN. INFO.: | | | US 1995-380682 | A2 19950215 |
| | | | WO 1996-US1114 | W 19960212 |
| | | | US 1997-894179 | A3 19970814 |

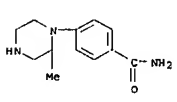
OTHER SOURCE(S): MARPAT 125:275875
GI



AB The title compds. (I; R1, R2 = H, halogen, alkyl, cycloalkyl, CN, (un)substituted CONH2, etc.; R3 = H, halogen, CN, OH, alkyl, CHO, etc.; R4-R7 = H, alkyl, cycloalkyl, cycloalkyl, (un)substituted aryl, etc.; R8-R10 = H, halogen, alkyl, cycloalkyl, CN, (un)substituted CONH2, (un)substituted NH2, etc.; W = N, CH; X = direct bond, NR4; Y = Ph, 2-, 3-, 4-pyridyl, pyrimidinyl, pyrazinyl, etc.] [e.g., 6-chloro-2-[[4-(4-methoxyphenyl)-1-piperazinyl]methyl]imidazo[1,2-a]pyridine; m.p. 111-112°], which are dopamine D4-receptor antagonists (e.g., I demonstrate a ki for displacement of 3H-spiperone from human dopamine D4 receptors of <2.5 μM), useful as antipsychotic (no data) and cardiovascular (no data) agents, are prepared

IT 182181-44-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of imidazo[1,2-a]pyridines dopamine D4-receptor antagonist cardiovascular and CNS agents)

RN 182181-44-8 CAPLUS
CN Benzamide, 4-(2-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



L9 ANSWER 46 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:494058 CAPLUS
DOCUMENT NUMBER: 125:142292
TITLE: Preparation of benzyloxyhydrazone derivatives as agrochemical fungicides
INVENTOR(S): Nishida, Tatsuki; Tajima, Sokichi; Tsubata, Kenji
PATENT ASSIGNEE(S): Nihon Nohyaku Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 56 pp.

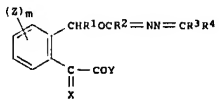


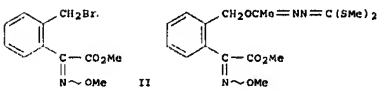


CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 08127563 | A | 19960521 | JP 1994-288799 | 19941029 <-- |
| PRIORITY APPLN. INFO.: | | | JP 1994-288799 | 19941029 |

OTHER SOURCE(S): MARPAT 125:142292
GI

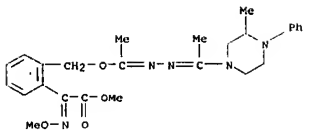




AB The title compds. [I; R1, R2 = H, C1-6 (halo)alkyl; R3, R4 = H, cyano, C1-6 (halo)alkyl, C3-6 cycloalkyl, etc.; X = CHOR5, NOR5 (wherein R5 = C1-6 alkyl); Y = C1-6 alkoxy, alkylthio, mono- or disubstituted amino; Z = halo, C1-6 (halo)alkyl; m = 0-4], effective agrochem. fungicides at low doses, are prepared Reaction of bromide II with AcNHN:C(SMe)2 in the presence of powdered KOH in DMSO at room temperature gave 42% hydrazone compound III, which showed 95-100% control of barley powdery mildew and Phytophthora infestans at 200 ppm.

IT 179935-74-1P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzyloxyhydrazone derivs. as agrochem. fungicides)

RN 179935-74-1 CAPLUS
CN Benzeneacetic acid, α-(methoxyimino)-2-[[1-[[3-methyl-4-phenyl-1-piperazinyl]ethylidene]hydrazono]ethoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)



L9 ANSWER 47 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:467020 CAPLUS
DOCUMENT NUMBER: 125:114630
TITLE: Certain 4-aminomethyl-2-substituted imidazole derivatives and 2-aminomethyl-4-substituted imidazole derivatives, new classes of dopamine receptor subtype specific ligands
INVENTOR(S): Thurkauf, Andrew; Horvath, Raymond F.; Yuan, Jun; Peterson, John M.
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9616040 | A1 | 19960530 | WO 1995-US15262 | 19951122 <-- |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5681956 | A | 19971028 | US 1995-401201 | 19950309 <-- |
| US 5633377 | A | 19970527 | US 1995-462833 | 19950605 <-- |
| US 5646281 | A | 19970708 | US 1995-461135 | 19950605 <-- |
| US 5656762 | A | 19970812 | US 1995-461858 | 19950605 <-- |
| US 5712392 | A | 19980127 | US 1995-464548 | 19950605 <-- |
| AU 9643689 | A | 19960617 | AU 1996-43689 | 19951122 <-- |
| ZA 9509910 | A | 19970822 | ZA 1995-9910 | 19951122 <-- |
| ZA 9509911 | A | 19970822 | ZA 1995-9911 | 19951122 <-- |
| EP 793653 | A1 | 19970910 | EP 1995-942473 | 19951122 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| ZA 9707500 | A | 19980223 | ZA 1997-7500 | 19951122 <-- |
| JP 10502670 | T | 19980310 | JP 1995-517074 | 19951122 <-- |
| JP 2941950 | B2 | 19990830 | | |
| BR 9509760 | A | 19980630 | BR 1995-9760 | 19951122 <-- |
| US 6069251 | A | 20000530 | US 1997-859861 | 19970521 <-- |
| US 6358955 | B1 | 20020319 | US 2000-497988 | 20000204 <-- |
| US 2002143044 | A1 | 20021003 | US 2002-100691 | 20020318 <-- |
| US 6797824 | B2 | 20040928 | | |

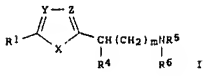
PRIORITY APPLN. INFO.: US 1994-344154 A2 19941123



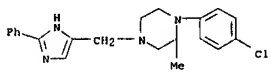


| | | |
|---|---|---|
| US 1994-344552 | A2 | 19941123 |
| US 1995-401201 | A2 | 19950309 |
| US 1990-635256 | A2 | 19901228 |
| US 1993-81317 | A2 | 19930108 |
| US 1994-313435 | A2 | 19940927 |
| US 1995-462833 | A1 | 19950605 |
| WO 1995-US15262 | W | 19951122 |
| US 1997-859861 | A1 | 19970521 |
| US 2000-497988 | A1 | 20000204 |

OTHER SOURCE(S): MARPAT 125:114630
GI



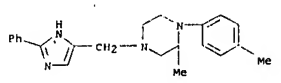
AB Disclosed are compds. (I), wherein R1 represents optionally substituted aryl, heteroaryl, arylalkyl, or cycloalkyl groups; X, Z, and Y are optionally substituted nitrogen or carbon atoms; R3 and R4 are organic or inorg. substituents which may together form ring structures; m is zero, one or two; and R5 and R6 are organic or inorg. substituents; and the pharmaceutically acceptable addition salts thereof, which compds. are highly selective partial agonists or antagonists at brain dopamine receptor subtypes or prodrugs thereof and are useful in the diagnosis and treatment of affective disorders such as schizophrenia and depression as well as certain movement disorders such as Parkinsonism. Specifically, 2-phenyl-4(5)-[(4-(2-pyrimidinyl)piperazin-1-yl)methyl]imidazole dihydrochloride was prepared and was shown to bind to the dopamine D4 receptor site (Ki = 1033, 8200, 2.7 for D2, D3, D4 binding sites, resp.).
IT 179333-05-2P 179333-06-3P 179333-36-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of imidazole derivs. as dopamine receptor partial agonists or antagonists for memory enhancement and treatment of schizophrenia and depression and Parkinsonism)
RN 179333-05-2 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl-4-[(2-phenyl-1H-imidazol-4-yl)methyl]- (9CI) (CA INDEX NAME)



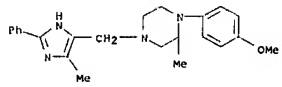
RN 179333-06-3 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)-4-[(2-phenyl-1H-imidazol-4-yl)methyl]- (9CI) (CA INDEX NAME)



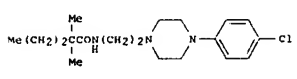




RN 179333-36-9 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl-4-[(5-methyl-2-phenyl-1H-imidazol-4-yl)methyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 48 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:368754 CAPLUS
DOCUMENT NUMBER: 125:104240
TITLE: N-(substituted-phenyl)piperazines: antagonists with high binding and functional selectivity for dopamine D4 receptors
AUTHOR(S): Boyfield, Izzy; Coldwell, Martyn C.; Hadley, Michael S.; Healy, Maureen A. M.; Johns, Amanda; Nash, David J.; Riley, Graham J.; Scott, Emma E.; Smith, Stephen A.; et al.
CORPORATE SOURCE: SmithKline Beecham Pharm., Harlow, CM19 5AW, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (1996), 6(11), 1227-1232
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

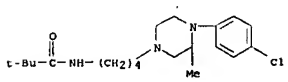


AB A series of N-(substituted-phenyl)piperazine derivs. was prepared as selective antagonists of the dopamine D4 receptor. Many analogs possessed a binding selectivity of over 100 fold for D4 over D2 receptors. In functional studies in the microphysiometer, compound I showed a selectivity over dopamine D2 receptors of greater than 1000 fold.
IT 179258-15-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of N-(substituted-phenyl)piperazines as D4 receptor antagonists in relation to schizophrenia)





RN 179258-15-2 CAPLUS
CN Propanamide, N-[4-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]butyl]-2,2-dimethyl- (9CI) (CA INDEX NAME)

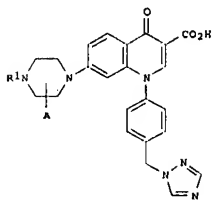


L9 ANSWER 49 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:225867 CAPLUS
DOCUMENT NUMBER: 124:261076
TITLE: Preparation of 7-piperazinyl-1,4-dihydro-4-oxo-1-[4-(1H-1,2,4-triazol-1-yl-methyl)phenyl]quinoline-3-carboxylic acids as virucides.
INVENTOR(S): Bender, Wolfgang; Roeben, Wolfgang; Paesens, Arnold; Bartel, Stephan
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 40 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 4425660 | A1 | 19960125 | DE 1994-4425660 | 19940720 <-- |
| WO 9602532 | A1 | 19960201 | WO 1995-EP2643 | 19950707 <-- |
| W: AU, CA, CN, CZ, FI, HU, JP, KR, LT, MX, NO, NZ, PL, RU, SI, SK, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9530763 | A | 19960216 | AU 1995-30763 | 19950707 <-- |
| ZA 9506012 | A | 19960222 | ZA 1995-6012 | 19950719 <-- |

PRIORITY APPLN. INFO.: DE 1994-4425660 A 19940720
WO 1995-EP2643 W 19950707

OTHER SOURCE(S): CASREACT 124:261076; MARPAT 124:261076
GI



AB Title compds. [I; A = H, Me; R1 = (substituted) Ph, naphthyl, pyridyl, pyrimidinyl, pyrazinyl, 3,4-methylenedioxyphenyl], were prepared Thus, 7-fluoro-1,4-dihydro-4-oxo-1-[4-(1H-1,2,4-triazol-1-ylmethyl)phenyl]-3-quinolinecarboxylic acid hydrochloride [preparation via 1-(4-aminobenzyl)-1H-1,2,4-triazole given] was stirred with 1-(o-fluorophenyl)piperazine and diisopropylamine in DMF at 120° to give 95.4% I (A = H; R1 = o-fluorophenyl). I inhibited HIV in human lymphocytes with IC50 = 0.08-0.7 μM.

IT 2946-76-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 7-piperazinyl-1,4-dihydro-4-oxo-1-[4-(1H-1,2,4-triazol-1-ylmethyl)phenyl]quinoline-3-carboxylic acids as virucides)

RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

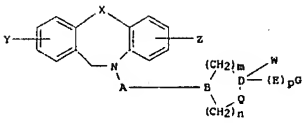
L9 ANSWER 50 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:958518 CAPLUS
DOCUMENT NUMBER: 124:146212
TITLE: 8-Chloro-10,11-dihydro-10-(1-piperazinylcarbonyl)dibenz[b,f][1,4]oxazepine derivatives and analogs as analgesics and prostaglandin-E2 antagonists
INVENTOR(S): Hansen, Donald W., Jr.; Peterson, Karen B.
PATENT ASSIGNEE(S): G. D. Searle and Co., USA
SOURCE: U.S., 38 pp. Cont.-in-part of U.S. 5,354,747.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5461047 | A | 19951024 | US 1994-245349 | 19940518 <-- |
| US 5354747 | A | 19941011 | US 1993-79021 | 19930616 <-- |
| CA 2165159 | A1 | 19941222 | CA 1994-2165159 | 19940602 <-- |
| WO 9429286 | A1 | 19941222 | WO 1994-US6029 | 19940602 <-- |
| W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TT, UA, US, UZ, VN | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9471387 | A | 19950103 | AU 1994-71387 | 19940602 <-- |
| EP 703908 | A1 | 19960403 | EP 1994-920687 | 19940602 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| JP 09500107 | T | 19970107 | JP 1994-501874 | 19940602 <-- |
| PRIORITY APPLN. INFO.: | | | US 1993-79021 | A2 19930616 |
| | | | US 1994-245349 | A 19940518 |
| | | | WO 1994-US6029 | W 19940602 |





OTHER SOURCE(S): CASREACT 124:146212; MARPAT 124:146212
GI



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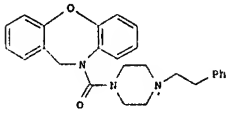


II

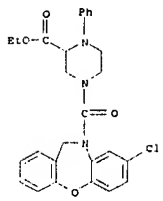
AB The present invention provides substituted dibenzoxazepine and dibenzothiazepine compds. I or a pharmaceutically-acceptable salt thereof, wherein: W = (H)r; Q = (CH(R)q)t; X is oxygen, sulfur, SO, or SO2; Y is hydrogen, halogen or hydroxy; Z is hydrogen or halogen; A is alkylene or carbonyl; B is CH or nitrogen; D is carbon or nitrogen; E is alkylene, carbonyl, alkyleneamino or alkylenecarbonyl; G is hydrogen, alkyl, cycloalkyl, alkoxy, aminoalkyl, aminocycloalkyl, aryl, alkylenearyl or aryl-substituted aryl; R is hydrogen or CO2R1 ; R1 is hydrogen or alkyl; m is an integer of from 0 to 4; n is an integer of from 0 to 4; r is 0 or 1; q is an integer of from 0 to 1; t is an integer of from 0 to 1; and p is an integer of from 0 to 1 (with provisos) which are useful as analgesic agents for the treatment of pain, and for prostaglandin-E2 mediated diseases. Thus, e.g., 10,11-dihydro-10-[[4-(2-phenylethyl)-1-piperazinyl]carbonyl]dibenz[b,f][1,4]oxazepine, monohydrochloride (II.HCl) was synthesized by reductive alkylation of 8-chloro-10,11-dihydro-10-(1-piperazinylcarbonyl)dibenz[b,f][1,4]oxazepine, monohydrochloride (preparation given) with phenylacetaldehyde, and exhibited analgesic activity of 10/10 in the writhing assay and prostaglandin-E2 antagonism with dose ratio of EC50 doses = 2.6.

IT 163839-09-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(8-chloro-10,11-dihydro-10-(1-piperazinylcarbonyl)dibenz[b,f][1,4]oxazepine derivs. and analogs as analgesics and prostaglandin-E2 antagonists)

RN 163839-09-6 CAPLUS
CN 2-Piperazinecarboxylic acid, 4-[(8-chlorodibenz[b,f][1,4]oxazepin-10(11H)-yl)carbonyl]-1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)

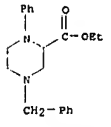




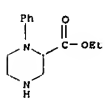


IT 162082-37-3P, Ethyl 1-phenyl-4-(phenylmethyl)-2-piperazinecarboxylate 162082-38-4P, Ethyl 1-phenyl-2-piperazinecarboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(8-chloro-10,11-dihydro-10-(1-piperazinylcarbonyl)dibenz[b,f][1,4]oxazepine derivs. and analogs as analgesics and prostaglandin-E2 antagonists)

RN 162082-37-3 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-4-(phenylmethyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 162082-38-4 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



L9 ANSWER 51 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:954796 CAPLUS

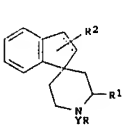




DOCUMENT NUMBER: 123:330860
TITLE: Tocolytic oxytocin receptor antagonists
INVENTOR(S): Bock, Mark G.; Evans, Ben E.; Culberson, J. Christopher; Gilbert, Kevin F.; Rittle, Kenneth E.; Williams, Peter D.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9525443 | A1 | 19950928 | WO 1995-US3738 | 19950323 <-- |
| W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, US, UZ | | | | |
| RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5464788 | A | 19951107 | US 1994-217270 | 19940324 <-- |
| CA 2186129 | A1 | 19950928 | CA 1995-2186129 | 19950323 <-- |
| AU 9521952 | A | 19951009 | AU 1995-21952 | 19950323 <-- |
| AU 686792 | B2 | 19980212 | | |
| EP 751773 | A1 | 19970108 | EP 1995-914875 | 19950323 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| JP 09512521 | T | 19971216 | JP 1995-524838 | 19950323 <-- |
| US 5756504 | A | 19980526 | US 1996-718415 | 19960923 <-- |
| PRIORITY APPLN. INFO.: | | | US 1994-217270 | A2 19940324 |
| | | | WO 1995-US3738 | W 19950323 |

OTHER SOURCE(S): MARPAT 123:330860
GI



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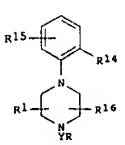


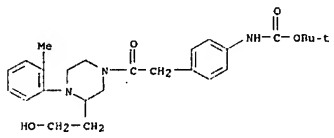
II

AB Spiroindenepiperidine derivs. I [R1 = H, C1-5 alkyl, CN, CO2H, Ph, etc.; R2 = H, PhCH2, C3-8 cycloalkyl, C1-5 alkyl; Y = CO2, C(O)NR2, C(:NR2), SO2, C(O)(CH2)n, (CH2)p, (CH2)pC(O); R = (tetrahydro)naphthyl, (substituted) cyclohexyl, (substituted) Ph, heterocyclyl; bond in cyclopentane ring is single or double; n = 0-3; p = 1-3] and phenylpiperazine derivs. II (Y, R, R1 as above; R14, R15 = H, C1-5 alkyl, C1-5 alkoxy, halo, NO2, CN; R16 = H, :O) and their pharmaceutically acceptable salts and esters are useful as oxytocin and vasopressin receptor antagonists for treatment of preterm labor and dysmenorrhea and for stopping labor prior to cesarean delivery. Thus, 1-[2-methoxy-4-[1-[2-

(N-cyclopropylamino)ethylsulfonyl]-4-piperidyloxy]phenylacetyl]-4-(2-methylphenyl)piperazine-2-carboxamide (III) was prepared in 11 steps from 4-hydroxypiperidine, Me 2,4-dihydroxybenzoate, 2-benzylaminoethanol, o-toluidine, 2,3-dibromopropionamide, and cyclopropylamine. III competed with 1 nM oxytocin-3H for binding to rat uterine tissue with an IC50 of 20 nM.

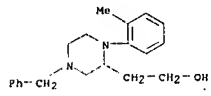
IT 170929-79-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tocolytic oxytocin receptor antagonists)

RN 170929-79-0 CAPLUS
CN Carbamic acid, [4-[2-[3-(2-hydroxyethyl)-4-(2-methylphenyl)-1-piperazinyl]-2-oxoethyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

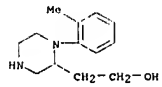


IT 170930-08-2P 170930-09-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(tocolytic oxytocin receptor antagonists)

RN 170930-08-2 CAPLUS
CN 2-Piperazineethanol, 1-(2-methylphenyl)-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 170930-09-3 CAPLUS
CN 2-Piperazineethanol, 1-(2-methylphenyl)- (9CI) (CA INDEX NAME)



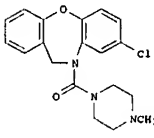




L9 ANSWER 52 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:682580 CAPLUS
DOCUMENT NUMBER: 123:83397
TITLE: Analgesic dibenzoxazepines and dibenzothiazepines
INVENTOR(S): Hansen, Donald Willis, Jr.; Peterson, Karen Berenice
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9429286 | A1 | 19941222 | WO 1994-US6029 | 19940602 <-- |
| W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TT, UA, US, UZ, VN | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5354747 | A | 19941011 | US 1993-79021 | 19930616 <-- |
| US 5461047 | A | 19951024 | US 1994-245349 | 19940518 <-- |
| AU 9471387 | A | 19950103 | AU 1994-71387 | 19940602 <-- |
| EP 703908 | A1 | 19960403 | EP 1994-920687 | 19940602 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| JP 09500107 | T | 19970107 | JP 1994-501874 | 19940602 <-- |
| PRIORITY APPLN. INFO.: | | | US 1993-79021 A | 19930616 |
| | | | US 1994-245349 A | 19940518 |
| | | | WO 1994-US6029 W | 19940602 |
| OTHER SOURCE(S): | MARPAT 123:83397 | | | |

GI



I

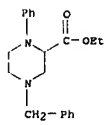
AB Dibenz[b,f][1,4]oxazepines and dibenz[b,f][1,4]thizepines were disclosed for the treatment of prostaglandin-E2 mediated diseases. A claimed example compound is 8-chloro-10,11-dihydro-10-[[4-(phenylmethyl)-1-piperazinyl]carbonyl]dibenz[b,f][1,4]oxazepine hydrochloride (I).

IT 162082-37-3P 162082-38-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of dibenz[b,f][1,4]oxazepines analgesics)

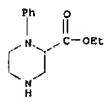
RN 162082-37-3 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-4-(phenylmethyl)-, ethyl ester (9CI) (CA INDEX NAME)





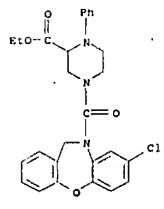


RN 162082-38-4 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



IT 163839-09-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dibenz[b,f][1,4]oxazepines analgesics)

RN 163839-09-6 CAPLUS
CN 2-Piperazinecarboxylic acid, 4-[(8-chlorodibenz[b,f][1,4]oxazepin-10(11H)-yl)carbonyl]-1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



L9 ANSWER 53 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:274966 CAPLUS
DOCUMENT NUMBER: 122:81403
TITLE: Preparation of 3-(piperazinomethyl)indazoles as dopaminergic antagonists
INVENTOR(S): Baker, Raymond; Kulagowski, Janusz Jozef; Leeson, Paul David; Smith, Adrian Leonard

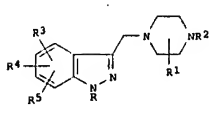




PATENT ASSIGNEE(S): Merck Sharp and Dohme Ltd., UK
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9421630 | A1 | 19940929 | WO 1994-GB504 | 19940314 <-- |
| W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, UA, US, UZ, VN | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2156838 | A1 | 19940929 | CA 1994-2156838 | 19940314 <-- |
| AU 9462140 | A | 19941011 | AU 1994-62140 | 19940314 <-- |
| AU 685090 | B2 | 19980115 | | |
| EP 689539 | A1 | 19960103 | EP 1994-909210 | 19940314 <-- |
| EP 689539 | B1 | 19971203 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| JP 08512284 | T | 19961224 | JP 1994-520766 | 19940314 <-- |
| AT 160779 | T | 19971215 | AT 1994-909210 | 19940314 <-- |
| ES 2110225 | T3 | 19980201 | ES 1994-909210 | 19940314 <-- |
| US 5780475 | A | 19980714 | US 1995-525629 | 19951229 <-- |
| PRIORITY APPLN. INFO.: | | | GB 1993-5623 A | 19930318 |
| | | | WO 1994-GB504 W | 19940314 |
| OTHER SOURCE(S): | MARPAT 122:81403 | | | |

GI

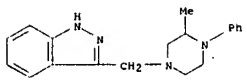


I

AB Title compds. [I; R = H, alkyl; R1 = H, (cyclo)alkyl, alkoxy, (hetero)aryl, etc.; R2 = (cyclo)alkyl, alkoxy, (hetero)aryl, etc.; R3-R5 = H, halo, cyano, hydrocarbyl, etc.] were prepared Thus, 1H-indazole-3-carboxylic acid was amidated by 1-(4-chlorophenyl)piperazine and the product reduced to give I (R = R1 = R3-R5 = H, R2 = 4-ClC6H4). I had Ki of 1.5μM for displacement of spiperone from cloned human dopamine D4 receptors in vitro.

IT 160008-87-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-(piperazinomethyl)indazoles as dopaminergic antagonists)

RN 160008-87-7 CAPLUS
CN 1H-Indazole, 3-[(3-methyl-4-phenyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)

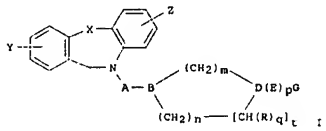


L9 ANSWER 54 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:205963 CAPLUS
DOCUMENT NUMBER: 123:9468
TITLE: 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9- and/or 10-substituted dibenzoxazepine and dibenzthiazepine compounds as analgesics and prostaglandin E2 antagonists, pharmaceutical compositions and methods of use
INVENTOR(S): Hansen, Donald W., Jr.; Peterson, Karen B.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 39 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5354747 | A | 19941011 | US 1993-79021 | 19930616 <-- |
| US 5461047 | A | 19951024 | US 1994-245349 | 19940518 <-- |
| CA 2165159 | A1 | 19941222 | CA 1994-2165159 | 19940602 <-- |
| WO 9429286 | A1 | 19941222 | WO 1994-US6029 | 19940602 <-- |
| W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TT, UA, US, UZ, VN | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9471387 | A | 19950103 | AU 1994-71387 | 19940602 <-- |
| EP 703908 | A1 | 19960403 | EP 1994-920687 | 19940602 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| JP 09500107 | T | 19970107 | JP 1994-501874 | 19940602 <-- |

PRIORITY APPLN. INFO.: US 1993-79021 A2 19930616
US 1994-245349 A 19940518
WO 1994-US6029 W 19940602

OTHER SOURCE(S): CASREACT 123:9468; MARPAT 123:9468
GI

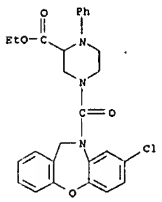


I





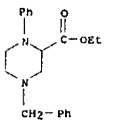
AB The present invention provides substituted dibenzoxazepine and dibenzthiazepine compds. I which are useful as analgesic agents for the treatment of pain, and for prostaglandin-E2 mediated diseases, pharmaceutical compns. comprising a therapeutically-effective amount of I in combination with a pharmaceutically-acceptable carrier, a method for eliminating or ameliorating pain in an animal comprising administering a therapeutically-effective amount of I to the animal, and a method for treating prostaglandin-E2 mediated diseases in an animal comprising administering a therapeutically-effective amount of I to the animal. Analgesic activity was measured using the writhing assay at standard dose of 10 mpk/g body weight; I produced analgesia in from 2/10 to 10/10 of the mice. Prostaglandin E2 antagonism assay (inhibition of contraction of guinea pig ileum); dose ratio of EC50 doses of from 0.8 to 32. Pharmaceutical compns. were given.
IT 163839-09-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(substituted dibenzoxazepine and dibenzthiazepine compds. as analgesics and prostaglandin E2 antagonists)
RN 163839-09-6 CAPLUS
CN 2-Piperazinecarboxylic acid, 4-[(8-chlorodibenz[b,f][1,4]oxazepin-10(11H)-yl)carbonyl]-1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



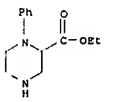
IT 162082-37-3P, Ethyl 1-Phenyl-4-(phenylmethyl)-2-piperazinecarboxylate 162082-38-4P, Ethyl 1-phenyl-2-piperazinecarboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(substituted dibenzoxazepine and dibenzthiazepine compds. as analgesics and prostaglandin E2 antagonists)
RN 162082-37-3 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-4-(phenylmethyl)-, ethyl ester (9CI) (CA INDEX NAME)







RN 162082-38-4 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



L9 ANSWER 55 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:205962 CAPLUS
DOCUMENT NUMBER: 122:239729
TITLE: Squaric acid derivatives of substituted dibenzoxazepine compounds as analgesics and prostaglandin E2 antagonists, pharmaceutical compositions and methods of use
INVENTOR(S): Chandrakumar, Nizal S.; Pitzele, Barnett S.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 18 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

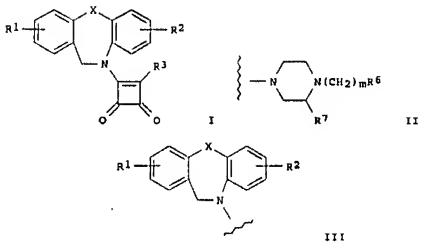
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5354746 | A | 19941011 | US 1993-69503 | 19930601 <-- |
| WO 9427981 | A1 | 19941208 | WO 1994-US4973 | 19940511 <-- |
| W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TT, UA, US, UZ, VN | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9467831 | A | 19941220 | AU 1994-67831 | 19940511 <-- |

PRIORITY APPLN. INFO.: US 1993-69503 A 19930601
WO 1994-US4973 W 19940511

OTHER SOURCE(S): MARPAT 122:239729
GI

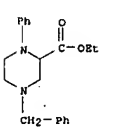




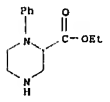


I II III

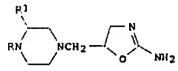
AB The present invention provides substituted dibenzoxazepine compds. of formula I (X = O, S, SO, SO2; R1, R2 = H, halogen; R3 = NR4R5, alkoxy, II, III; R4 = H, alkyl; R5 = alkyl, alkylene-NR4R4, alkylaryl; R6 = Me, aryl; R7 = H, CO2R4; m = 0-5) which are useful as analgesic agents for the treatment of pain, and as prostaglandin-E2 antagonists for the treatment of prostaglandin-E2 mediated diseases, pharmaceutical compns. comprising a therapeutically-effective amount of a compound I in combination with a pharmaceutically-acceptable carrier, a method for eliminating or ameliorating pain in an animal, and a method for treating prostaglandin-E2 mediated diseases in an animal, comprising administering a therapeutically-effective amount of a compound I Formula I to the animal. Analgesic activity assessed by writhing assay at 30 mg/kg dose: in from 4/10 to 6/10 of mice, the number of writhes elicited by PBQ was equal to, or less than, one-half the median number of writhes recorded for the saline-treated control group. PGE2 antagonism assay: EC50 dose ratios of 1.9 ± 0.9 to 153 ± 74 for inhibition of contraction of guinea pig ileum. Pharmaceutical formulations were given.
IT 162082-37-3P, Ethyl 1-phenyl-4-(phenylmethyl)-2-piperazinecarboxylate 162082-38-4P, Ethyl 1-phenyl-2-piperazinecarboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(squaric acid derivs. of substituted dibenzoxazepine compds. as analgesics and prostaglandin E2 antagonists)
RN 162082-37-3 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-4-(phenylmethyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 162082-38-4 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



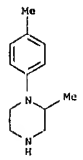
L9 ANSWER 56 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:457460 CAPLUS
DOCUMENT NUMBER: 121:57460
TITLE: 2-Amino-2-oxazolines. VII. Influence of structural parameters on the antidepressant activity of 5-(1-aryl-4-piperazino)methyl-2-amino-2-oxazolines
AUTHOR(S): Bosc, Jean Jacques; Forfar, Isabelle; Jarry, Christian; Laguerre, Michel; Carpy, Alain
CORPORATE SOURCE: Lab. Chim. Phys., Univ. Bordeaux II, Bordeaux, 33076, Fr.
SOURCE: Archiv der Pharmazie (Weinheim, Germany) (1994), 327(3), 187-92
CODEN: ARPMAS; ISSN: 0365-6233
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 121:57460
GI



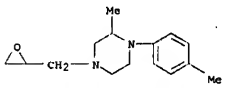
AB [(Arylpiperazino)methyl]aminooxazolines I (R = substituted Ph, R1 = H, Me) were prepared and screened for antidepressant activity. Their lipophilic behavior is discussed in relation to the nature and the position of substituents on the aromatic ring. The influence of steric effects on the pharmacol. activity has been investigated using exptl. methods (x-ray diffraction, NMR) and theor. calcns. (semi-empirical quantum mechanics). Ortho-substitution on the Ph ring or C(α)-substitution on the piperazine ring by a Me group results in the same effects, i.e., an increase of the angle between the two rings up to 64° (x-ray and calcn.) and a loss of antidepressant activity.
IT 35947-11-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation by, of epichlorohydrin)
RN 35947-11-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)- (CA INDEX NAME)





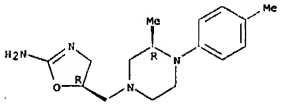


IT 155850-87-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and cleavage of, with monosodium cyanamide)
RN 155850-87-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)-4-(oxiranylmethyl)- (9CI) (CA INDEX NAME)



IT 155850-82-1P 155850-86-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, antidepressant activity, and NMR of)
RN 155850-82-1 CAPLUS
CN 2-Oxazolamine, 4,5-dihydro-5-[[3-methyl-4-(4-methylphenyl)-1-piperazinyl]methyl]-, (R*,R*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

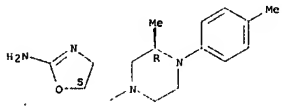


RN 155850-86-5 CAPLUS
CN 2-Oxazolamine, 4,5-dihydro-5-[[3-methyl-4-(4-methylphenyl)-1-piperazinyl]methyl]-, (R*,S*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.







L9 ANSWER 57 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:8618 CAPLUS
DOCUMENT NUMBER: 120:8618
TITLE: Alkyl derivatives of trazodone with CNS activity and reduced side effects
INVENTOR(S): Baiocchi, Leandro
PATENT ASSIGNEE(S): Istituto Ricerca Francesco Angelini S.p.A., Italy
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| WO 9314091 | A1 | 19930722 | WO 1993-EP80 | 19930114 | <-- |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG | | | | | |
| AU 9333504 | A | 19930803 | AU 1993-33504 | 19930114 | <-- |
| AU 671973 | B2 | 19960919 | | | |
| EP 623131 | A1 | 19941109 | EP 1993-902204 | 19930114 | <-- |
| EP 623131 | B1 | 19960403 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | | |
| JP 07503000 | T | 19950330 | JP 1993-512150 | 19930114 | <-- |
| JP 2856912 | B2 | 19990210 | | | |
| HU 70761 | A2 | 19951030 | HU 1994-2119 | 19930114 | <-- |
| HU 218678 | B | 20001028 | | | |
| AT 136307 | T | 19960415 | AT 1993-902204 | 19930114 | <-- |
| HU 72591 | A2 | 19960528 | HU 1995-2179 | 19930114 | <-- |
| HU 217968 | B | 20000528 | | | |
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| BR 9305752 | A | 19970128 | BR 1993-5752 | 19930114 | <-- |
| PL 170913 | B1 | 19970228 | PL 1993-304665 | 19930114 | <-- |
| CZ 282910 | B6 | 19971112 | CZ 1994-1732 | 19930114 | <-- |
| RO 113465 | B1 | 19980730 | RO 1994-1203 | 19930114 | <-- |
| RU 2126801 | C1 | 19990227 | RU 1994-36769 | 19930114 | <-- |
| SK 280561 | B6 | 20000313 | SK 1994-846 | 19930114 | <-- |
| CA 2128202 | C | 20010123 | CA 1993-2128202 | 19930114 | <-- |
| ZA 9300292 | A | 19930819 | ZA 1993-292 | 19930115 | <-- |
| FI 9403386 | A | 19940715 | FI 1994-3386 | 19940715 | <-- |
| FI 110186 | B1 | 20021213 | | | |
| NO 9402668 | A | 19940916 | NO 1994-2668 | 19940715 | <-- |
| NO 302365 | B1 | 19980223 | | | |
| US 5543563 | A | 19960806 | US 1995-457490 | 19950601 | <-- |
| US 5739134 | A | 19980414 | US 1995-457114 | 19950601 | <-- |
| HU 71511 | A2 | 19951228 | HU 1995-2177 | 19950719 | <-- |
| HU 219493 | B | 20010428 | | | |





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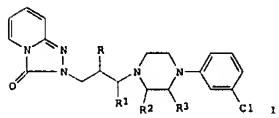
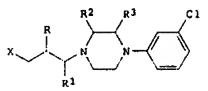
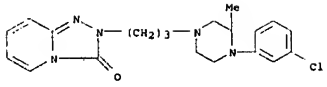
|---|---|---|---|---|---|
| HU 71512 | A2 | 19951228 | HU 1995-2178 | 19950719 | <-- |
| HU 217981 | B | 20000528 | | | |
| HU 71513 | A2 | 19951228 | HU 1995-2180 | 19950719 | <-- |
| HU 217982 | B | 20000528 | | | |
| US 5726178 | A | 19980310 | US 1996-758556 | 19961129 | <-- |
| NO 9704462 | A | 19940916 | NO 1997-4462 | 19970926 | <-- |
| FI 2002001652 | A | 20020916 | FI 2002-1652 | 20020916 | <-- |
| FI 113266 | B1 | 20040331 | | | |
| PRIORITY APPLN. INFO.: | | | IT 1992-MI84 | A 19920117 | |
| | | | HU 1994-2119 | A 19930114 | |
| | | | WO 1993-EP80 | A 19930114 | |
| | | | US 1994-256352 | A3 19940718 | |

OTHER SOURCE(S): MARPAT 120:8618
GI

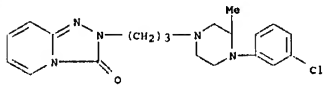




AB The title compds. I (only one of R, R1-R3 is C1-3 alkyl and the others are H), useful in the treatment of depression, and which have reduced affinity for adrenergic receptors thus not producing the side effects of trazodone (e.g., hypotension and priapism), are prepared by reacting 1,2,4-triazolo[4,3-a]pyridon-3-(2H)-one or its salts with alkali metal and with piperazine derivative II (X = leaving group). Thus, the Na salt of 1,2,4-triazolo[4,3-a]pyridin-3-2H)-one was condensed with 1-(3-chlorophenyl)-4-(3-chloro-2-methylpropyl)piperazine, producing I (R = Me, R1-R3 = H) hydrochloride salt, m.p. 196-198°, which demonstrated 27% inhibition of adrenergic α1-receptors at 10-7 M and 88% inhibition at 10-5 M, vs. 49% and 98%, resp., for trazodone.
IT 151448-01-0P 151448-02-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antidepressant with reduced adrenergic receptor affinity and side effects)
RN 151448-01-0 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyridin-3(2H)-one, 2-[3-[4-(3-chlorophenyl)-3-methyl-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)



RN 151448-02-1 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyridin-3(2H)-one, 2-[3-[4-(3-chlorophenyl)-3-methyl-1-piperazinyl]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L9 ANSWER 58 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:517276 CAPLUS
DOCUMENT NUMBER: 119:117276
TITLE: Novel 4-arylpiperazines and 4-arylpiperidines
INVENTOR(S): Reitz, Allen B.
PATENT ASSIGNEE(S): McNeilab, Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| WO 9304682 | A1 | 19930318 | WO 1992-US7754 | 19920911 | <-- |
| W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MG, MW, NO, RO, RU, SD | | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG | | | | | |
| ZA 9109629 | A | 19931206 | ZA 1991-9629 | 19911205 | <-- |
| HU 68963 | A2 | 19950828 | HU 1993-1362 | 19911220 | <-- |
| HU 217068 | B | 19991129 | | | |
| AU 9226599 | A | 19930405 | AU 1992-26599 | 19920911 | <-- |
| AU 657799 | B2 | 19950323 | | | |
| EP 563345 | A1 | 19931006 | EP 1992-920313 | 19920911 | <-- |
| EP 563345 | B1 | 20020703 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE | | | | | |
| HU 64535 | A2 | 19940128 | HU 1993-1361 | 19920911 | <-- |
| JP 06502870 | T | 19940331 | JP 1993-505525 | 19920911 | <-- |
| JP 2941945 | B2 | 19990830 | | | |
| RU 2139867 | C1 | 19991020 | RU 1993-41055 | 19920911 | <-- |
| SG 70980 | A1 | 20000321 | SG 1996-5506 | 19920911 | <-- |
| AT 219938 | T | 20020715 | AT 1992-920313 | 19920911 | <-- |





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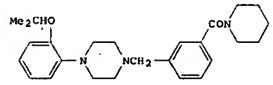
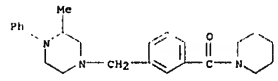
|---|---|---|---|---|---|
| ES 2179822 | T3 | 20030201 | ES 1992-920313 | 19920911 | |
| NO 9301695 | A | 19930527 | NO 1993-1695 | 19930510 | <-- |
| NO 9301694 | A | 19930630 | NO 1993-1694 | 19930510 | <-- |
| NO 303780 | B1 | 19980831 | | | |
| FI 111639 | B1 | 20030829 | FI 1993-2104 | 19930510 | |
| US 5569659 | A | 19961029 | US 1995-442600 | 19950517 | <-- |
| PRIORITY APPLN. INFO.: | | | US 1991-757881 | A 19910911 | |
| | | | US 1992-944006 | B1 19920911 | |
| | | | WO 1992-US7754 | A 19920911 | |
| | | | WO 1992-US9082 | W 19921220 | |
| | | | US 1994-365978 | B1 19941228 | |

OTHER SOURCE(S): MARPAT 119:117276
GI



I

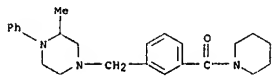
AB Title compds.4-RX(CH2)nCR1R2X1WNR3R4 [X = (un)substituted piperazino, piperidino; X1 = (un)substituted Ph; R = aryl; CR1R2 = CH2, CO, 1,1-alkanediyl, CHOH; W = CO, CS, SO2; NR3R4 = amino; n = 0-4] (113 compds.) were prepared as antipsychotic agents. Thus, 3-ClCH2C6H4COCl was treated with piperidine and N-(2-isopropoxyphenyl)piperazine to give the piperazine I which had an ED50 against apomorphine-induced emesis in dogs of 0.038mg/kg orally in dogs 1h before treatment with apomorphine..
IT 148826-90-8P 148853-59-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antipsychotic activity of)
RN 148826-90-8 CAPLUS
CN Piperidine, 1-[3-[(3-methyl-4-phenyl-1-piperazinyl)methyl]benzoyl]- (9CI) (CA INDEX NAME)



RN 148853-59-2 CAPLUS
CN Piperidine, 1-[3-[(3-methyl-4-phenyl-1-piperazinyl)methyl]benzoyl]-, monohydrochloride (9CI) (CA INDEX NAME)



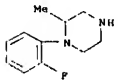




● HCl

IT 2946-76-1 148888-23-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation from; of antipsychotic arylpiperidines and arylpiperazines)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

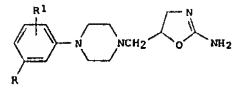
RN 148888-23-7 CAPLUS
CN Piperazine, 1-(2-fluorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



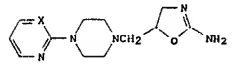
L9 ANSWER 59 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:182780 CAPLUS
DOCUMENT NUMBER: 118:182780
TITLE: RP-HPLC of new antidepressant 2-amino-2-oxazolines: a comparative study of their lipophilicity
AUTHOR(S): Desmotes-Mainard, F.; Thomas, J.; Bosc, J. J.; Devaux, G.; Jarry, C.
CORPORATE SOURCE: Dep. Pharmacol. Clin., CHR Pellegrin, Fr.
SOURCE: Journal of Liquid Chromatography (1993), 16(3), 767-76
CODEN: JLCHD8; ISSN: 0148-3919
DOCUMENT TYPE: Journal
LANGUAGE: English
GI





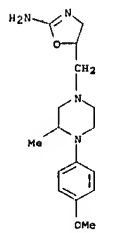


I



II

AB A comparative study of lipophilicity in a series of 5-(1-aryl-4-piperazino)methyl-2-amino-2-oxazolines, i.e., I (R = H, Me; R1 = H, Cl, F, Me, MeO, EtO, OH, CF3, Me2CH, NMe2, etc.) and II (X = CH, N), with antidepressant activity has been carried out using a RP-HPLC technique. This chromatog. method allowed the determination of log k'w values (k' = chromatog. column capacity factor) through extrapolation to 100% water from capacity factors data. The partition coeffs. (log Po/w) and ionization consts. (pKa) were measured by classical methods. A good correlation between log Po/w and log k'w was found, confirming the feasibility of using the latter as a lipophilicity descriptor. In this homogeneous chemical series the nature and the position of the substituents on the aromatic ring did not induce important variations on the pKa values, whereas they accounted for a great part in lipophilicity data.
IT 144881-48-1
RL: PRP (Properties)
(lipophilicity of, HPLC study of, structure in relation to)
RN 144881-48-1 CAPLUS
CN 2-Oxazolamine, 4,5-dihydro-5-[[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 60 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:38880 CAPLUS
DOCUMENT NUMBER: 118:38880

TITLE: Synthesis and antidepressant activity of 5-(1-aryl-4-piperazino)methyl-2-amino-2-oxazolines
AUTHOR(S): Bosc, J. J.; Jarry, C.; Carpy, A.; Panconi, E.; Descas, P.
CORPORATE SOURCE: Lab. Chim. Phys., Univ. Bordeaux II, Bordeaux, 33076, Fr.
SOURCE: European Journal of Medicinal Chemistry (1992), 27(5), 437-42
CODEN: EJMCA5; ISSN: 0223-5234
DOCUMENT TYPE: Journal
LANGUAGE: English
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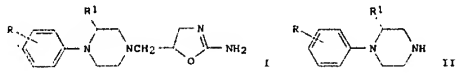
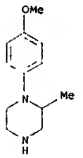


AB The synthesis of 20 5-(1-aryl-4-piperazino)methyl-2-amino-2-oxazolines, e.g., I (R = H, 2-, 3-, 4-Cl, 3,4-Cl2, 3-, 4-Me, 4-MeO, 4-Me2N; R1 = H, Me), from arylpiperazines II and epichlorhydrin is described. I(R = H, 4-OMe, 4-OH, 4-OAc, R1 = H) had ED50 <20mg/kg orally in the reserpine-induced hypothermia test in mice. Structure-activity relationships were studied and correlated with the nature of the aromatic substituent. Preliminary lipophilic and electronic properties of I (R, R1 = H) are reported.

IT 35947-12-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(addition reaction of, with epichlohydrin in synthesis of arylpiperazinylmethylaminooxazoline)

RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



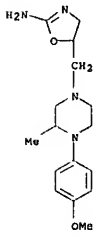
IT 144881-48-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antidepressant activity of)

RN 144881-48-1 CAPLUS
CN 2-Oxazolamine, 4,5-dihydro-5-[[4-(4-methoxyphenyl)-3-methyl-1-

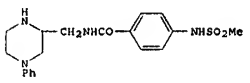




piperazinyl]methyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 61 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:106235 CAPLUS
DOCUMENT NUMBER: 116:106235
TITLE: Synthesis, cardiac electrophysiology, and β-blocking activity of novel arylpiperazines with potential as class II/III antiarrhythmic agents
AUTHOR(S): Phillips, Gary B.; Morgan, Thomas K., Jr.; Lumma, William C., Jr.; Gomez, Robert P.; Lind, Joan M.; Lis, Randall; Argentieri, Thomas; Sullivan, Mark E.
CORPORATE SOURCE: Dep. Med. Chem., Berlex Lab., Inc., Cedar Knolls, NJ, 07927, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(4), 743-50
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 116:106235
GI



AB Cyclocondensation reaction of N-aryl-N'-(phenylmethyl)-1,2-ethanediamine with 2,3-dibromopropionamide followed by derivatization gave a series of novel arylpiperazines, e.g., I. Thus, the key step in the preparation of the new compds. involves a regioselective heterocyclic ring formation. These were prepared in an attempt to incorporate both class II (β-receptor blocking) and class III antiarrhythmic properties in a single mol. All but four compds. significantly prolonged action potential duration in

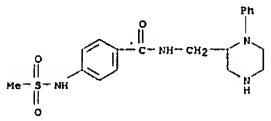




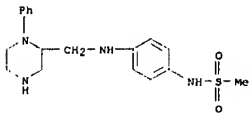
canine cardiac Purkinje fibers (class III activity). All but one of the compds. demonstrated β-receptor affinity in a competitive binding assay and three had β1-receptor selectivity. Compared to sotalol, a reference class II/III agent, I demonstrated β1-selectivity and was 1 order of magnitude more potent in the in vitro class III and the β1-receptor screens. I was evaluated further and found to be effective in preventing programmed elec. stimulation-induced arrhythmias in conscious dogs (class III activity) and against epinephrine-induced arrhythmias in halothane anesthetized dogs (class II activity).

IT 135036-09-8P 135036-10-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antiarrhythmic activity of)

RN 135036-09-8 CAPLUS
CN Benzamide, 4-[(methylsulfonyl)amino]-N-[(1-phenyl-2-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



RN 135036-10-1 CAPLUS
CN Methanesulfonamide, N-[4-[[(1-phenyl-2-piperazinyl)methyl]amino]phenyl]- (9CI) (CA INDEX NAME)

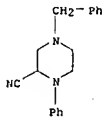


IT 135036-22-5P 135063-15-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

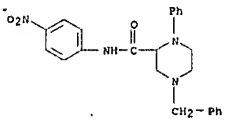
RN 135036-22-5 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)







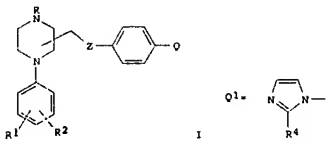
RN 135063-15-9 CAPLUS
CN 2-Piperazinecarboxamide, N-(4-nitrophenyl)-1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



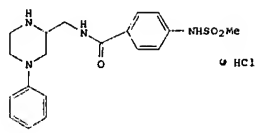
L9 ANSWER 62 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:471649 CAPLUS
DOCUMENT NUMBER: 115:71649
TITLE: Preparation of N-arylpiperazinylmethylamides as antiarrhythmics.
INVENTOR(S): Lumma, William Carl, Jr.; Morgan, Thomas Kenneth, Jr.; Phillips, Gary Bruce
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9104250 | A1 | 19910404 | WO 1990-EP1059 | 19900702 <-- |
| W: CA, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE | | | | |
| US 5051422 | A | 19910924 | US 1989-408020 | 19890915 <-- |
| CA 2067156 | A1 | 19910316 | CA 1990-2067156 | 19900702 <-- |
| EP 491709 | A1 | 19920701 | EP 1990-911657 | 19900702 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE | | | | |
| JP 05500660 | T | 19930212 | JP 1990-510812 | 19900702 <-- |
| US 5223623 | A | 19930629 | US 1991-757741 | 19910911 <-- |
| PRIORITY APPLN. INFO.: | | | US 1989-408020 A | 19890915 |
| | | | WO 1990-EP1059 W | 19900702 |

OTHER SOURCE(S): CASREACT 115:71649; MARPAT 115:71649
GI



I

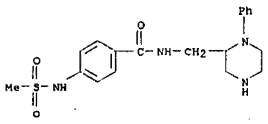


II

AB Title compds. (I; R = H, alkyl, PhCH2; R1, R2 = alkyl, alkoxy, halo; Z = NR3CO, NR3CH2, OCH2, NR3, NR3SO2; Q = alkylsulfonylimino, Q1; R3 = H, alkyl, allyl, alkoxyalkyl; R4 = H, Me), were prepared as cardiovascular agents, primarily antiarrhythmics (no data). Thus, 4-[(methylsulfonyl)amino]-N-[[4-phenyl-1-(phenylmethyl)piperazin-2-yl]methyl]benzamide hydrochloride was hydrogenolzed in MeOH over Pd(OH)2 to give title compound II.

IT 135036-09-8P 135036-10-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antiarrhythmic)

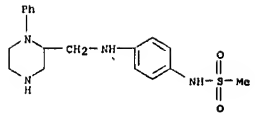
RN 135036-09-8 CAPLUS
CN Benzamide, 4-[(methylsulfonyl)amino]-N-[(1-phenyl-2-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



RN 135036-10-1 CAPLUS
CN Methanesulfonamide, N-[4-[[(1-phenyl-2-piperazinyl)methyl]amino]phenyl]- (9CI) (CA INDEX NAME)

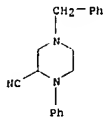




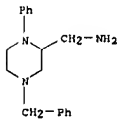


IT 135036-22-5P 135036-23-6P 135036-24-7P
135036-33-8P 135036-42-9P 135036-43-0P
135063-15-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for antiarrhythmic)

RN 135036-22-5 CAPLUS
CN 2-Piperazinecarbonitrile, 1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



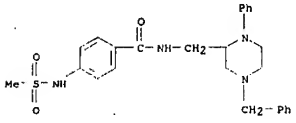
RN 135036-23-6 CAPLUS
CN 2-Piperazinemethanamine, 1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



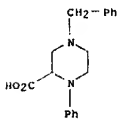
RN 135036-24-7 CAPLUS
CN Benzamide, 4-[(methylsulfonyl)amino]-N-[[1-phenyl-4-(phenylmethyl)-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



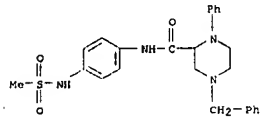




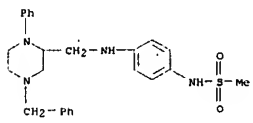
RN 135036-33-8 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 135036-42-9 CAPLUS
CN 2-Piperazinecarboxamide, N-[4-[(methylsulfonyl)amino]phenyl]-1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



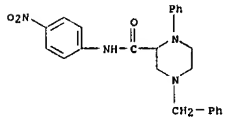
RN 135036-43-0 CAPLUS
CN Methanesulfonamide, N-[4-[[[1-phenyl-4-(phenylmethyl)-2-piperazinyl]methyl]amino]phenyl]- (9CI) (CA INDEX NAME)





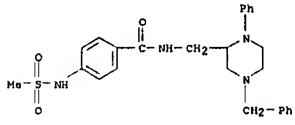


RN 135063-15-9 CAPLUS
CN 2-Piperazinecarboxamide, N-(4-nitrophenyl)-1-phenyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



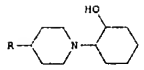
IT 135036-24-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of antiarrhythmic)

RN 135036-24-7 CAPLUS
CN Benzamide, 4-[(methylsulfonyl)amino]-N-[[1-phenyl-4-(phenylmethyl)-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 63 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 1989:231402 CAPLUS |
| DOCUMENT NUMBER: | 110:231402 |
| TITLE: | Synthesis, in vitro acetylcholine-storage-blocking activities, and biological properties of derivatives and analogs of trans-2-(4-phenylpiperidino)cyclohexanol (vesamicol) |
| AUTHOR(S): | Rogers, Gary A.; Parsons, Stanley M.; Anderson, D. C.; Nilsson, Lena M.; Bahr, Ben A.; Kornreich, Wayne D.; Kaufman, Rose; Jacobs, Robert S.; Kirtman, Bernard |
| CORPORATE SOURCE: | Dep. Chem., Univ. California, Santa Barbara, CA, 93106, USA |
| SOURCE: | Journal of Medicinal Chemistry (1989), 32(6), 1217-30 CODEN: JMCMAR; ISSN: 0022-2623 |
| DOCUMENT TYPE: | Journal |
| LANGUAGE: | English |
| OTHER SOURCE(S): | CASREACT 110:231402 |
| GI | |



AB Eighty-four analogs, e.g., I [R = (un)substituted Ph, cyclohexyl, PhCH2, Ph(CH2)3] and derivs. of the acetylcholine storage-blocking drug trans-2-4(4-phenylpiperidino)cyclohexanol (vesamicol) were synthesized, and their potencies were evaluated with the acetylcholine active-transport assay utilizing purified synaptic vesicles from Torpedo elec. organ. The parent drug exhibits enantioselectivity, with (-)-vesamicol being 25-fold more potent than (+)-vesamicol. The mol. structure and absolute configuration of (+)-vesamicol were determined by x-ray crystallog. The absolute configuration
of (-)-vesamicol is (1R,2R). Structure-activity evidence indicates that (-)-vesamicol does not act as an acetylcholine analog. Alterations to all three rings can have large effects on potency. Unexpectedly, analogs locking the alc. and ammonium groups trans-diequatorial or trans-diaxial both exhibit good potency. A potent benzovesamicol family was discovered that is suitable for facile elaboration of the sort useful in affinity labeling and affinity chromatog. applications. A good correlation was found between potencies as assessed by the acetylcholine transport assay and LD50 values in mouse.

IT 2946-76-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with cyclohexene epoxide)

RN 2946-76-1 CAPLUS

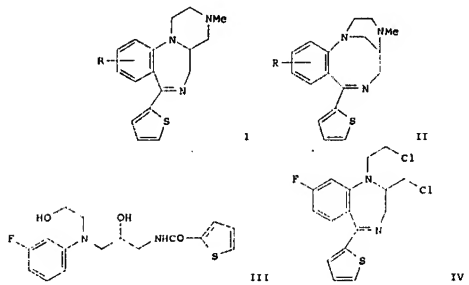
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

L9 ANSWER 64 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:189237 CAPLUS
DOCUMENT NUMBER: 110:189237
TITLE: Synthesis and antimicrobial activity of some pyrrole derivatives. III. 2-(4-Arylpiperazino)-3-ethoxycarbonyl-5-arylpyrrole derivatives
AUTHOR(S): Cocco, M. T.; Congiu, C.; Maccioni, A.; Schivo, M. L.; De Logu, A.; Palmieri, G.
CORPORATE SOURCE: Ist. Chim. Farm. Tossicol. Appl., Univ. Cagliari, Cagliari, Italy
SOURCE: Farmaco, Edizione Scientifica (1988), 43(12), 951-60
CODEN: FRPSAX; ISSN: 0430-0920
DOCUMENT TYPE: Journal
LANGUAGE: English
GI





OTHER SOURCE(S): CASREACT 110:173198
GI

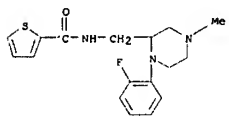


AB The pyrazinobenzodiazepine derivs. I (R = 9-, 10-, 11-F, 11-Me, 11-MeO) and (iminoethano)benzodiazocine deriv. II (R = 7-, 8-, 9-F) were prepared Thus, the amide III was cyclized by POCl3 to give the benzodiazepine IV, which was cyclized with MeNH2 to give I (R = 10-F). I and II exhibited pronounced antipsychotic activity. The influence of fluorosubstitution and variation of the fused ring system were measured.

IT 120107-24-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization reaction of, pyrazinobenzodiazepine derivative from)

RN 120107-24-6 CAPLUS

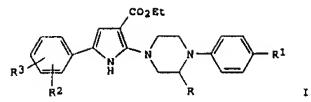
CN 2-Thiophenecarboxamide, N-[[1-(2-fluorophenyl)-4-methyl-2-piperazinyl]methyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl





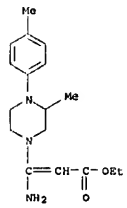


AB The synthesis of the title compds. (I, R = H, Me; R1 = H, halo; R2 = H, OMe, halo, NO2, alkyl; R3 = halo, Me, OMe) is described. The in vitro biol. investigation showed that I (R = R1 H; R2 = 3-NO2; R3 = 4-Cl) had considerable antibacterial activity against gram-pos. microorganisms and antifungal activity against Candida rugosa, while the other I did not show significant activity.

IT 120244-18-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 120244-18-0 CAPLUS

CN 2-Propenoic acid, 3-amino-3-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]-, ethyl ester (CA INDEX NAME)



L9 ANSWER 65 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:173198 CAPLUS
DOCUMENT NUMBER: 110:173198
TITLE: 1,4-Benzodiazepines and 1,5-benzodiazocines. XI. Synthesis and biological activity
AUTHOR(S): Heitmann, Walter; Liepmann, Hans; Maetzel, Uwe; Zeugner, Horst; Fuchs, Andreas M.; Kraehling, Hermann; Ruhland, Michael; Mol, Frans; Tulp, Martin T. M.
CORPORATE SOURCE: Pharm. Div., Kali-Chemie A.-G., Hannover, D-3000, Fed. Rep. Ger.
SOURCE: European Journal of Medicinal Chemistry (1988), 23(3), 249-56
CODEN: EJMCA5; ISSN: 0223-5234
DOCUMENT TYPE: Journal
LANGUAGE: English

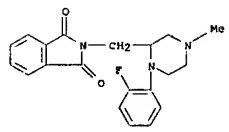




IT 120107-04-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and hydrazonolysis of)

RN 120107-04-2 CAPLUS

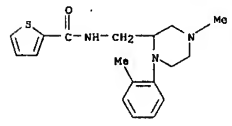
CN 1H-Isoindole-1,3(2H)-dione, 2-[[1-(2-fluorophenyl)-4-methyl-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



IT 120107-10-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and intramol. cyclization of, pyrazinobenzodiazepine derivative from)

RN 120107-10-0 CAPLUS

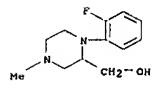
CN 2-Thiophenecarboxamide, N-[[4-methyl-1-(2-methylphenyl)-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



IT 120107-03-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and mesylation of)

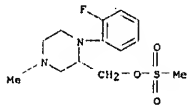
RN 120107-03-1 CAPLUS

CN 2-Piperazinemethanol, 1-(2-fluorophenyl)-4-methyl- (9CI) (CA INDEX NAME)

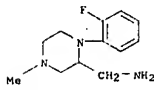


IT 120107-22-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

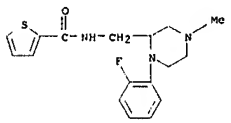
(preparation and reaction with potassium phthalimide)
RN 120107-22-4 CAPLUS
CN 2-Piperazinemethanol, 1-(2-fluorophenyl)-4-methyl-, methanesulfonate (ester) (9CI) (CA INDEX NAME)



IT 120107-23-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with thiophenecarbonyl chloride)
RN 120107-23-5 CAPLUS
CN 2-Piperazinemethanamine, 1-(2-fluorophenyl)-4-methyl- (9CI) (CA INDEX NAME)



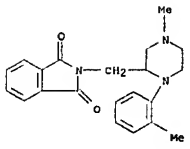
IT 120107-05-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 120107-05-3 CAPLUS
CN 2-Thiophenecarboxamide, N-[[1-(2-fluorophenyl)-4-methyl-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



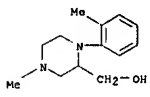
IT 120107-09-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, hydrazinolysis, and reaction with thiophenecarbonyl chloride)
RN 120107-09-7 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[[4-methyl-1-(2-methylphenyl)-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)







IT 120107-08-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, mesylation, and reaction with potassium phthalimide)
RN 120107-08-6 CAPLUS
CN 2-Piperazinemethanol, 4-methyl-1-(2-methylphenyl)- (9CI) (CA INDEX NAME)



L9 ANSWER 66 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:601296 CAPLUS
DOCUMENT NUMBER: 109:201296
TITLE: Photographic material for light-stable images
INVENTOR(S): Yoshimoto, Shinji; Nakagawa, Satoshi; Kaneko, Yutaka; Sugita, Shuichi; Shimada, Naoko
PATENT ASSIGNEE(S): Konica Co., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 18 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

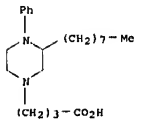
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 63101848 | A | 19880506 | JP 1986-246728 | 19861017 <-- |
| PRIORITY APPLN. INFO.: | | | JP 1986-246728 | 19861017 |

GI For diagram(s), see printed CA Issue.
AB A Ag halide photog. material contains ≥1 magenta couples I [Z = atom required to complete N heterocycle; X = H, group releasable on reacting with oxidized form of color developing agent; R = H, substituent] and an image stabilizer II [R21 = SO3M, CO2M; M = H, monovalent metal; X = divalent organic group; Z = atoms required to form 5-7-membered N heterocycle]. Light-stable images are obtained and staining and fogging are minimized.
IT 117209-45-7





RL: USES (Uses)
(magenta image stabilizer, for light stability)
RN 117209-45-7 CAPLUS
CN 1-Piperazinebutanoic acid, 3-octyl-4-phenyl- (9CI) (CA INDEX NAME)



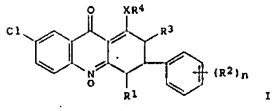
L9 ANSWER 67 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:473142 CAPLUS
DOCUMENT NUMBER: 109:73142
TITLE: New 1-substituted 3-aryl-7-chloro-3,4-dihydro-2H-acridone N-oxides, a procedure for their preparation, formulations containing them, and their use as pharmaceuticals and feed additives
INVENTOR(S): Dhar, Rajkumar; Venugopalan, Bindumadhavan; Chatterjee, Dipak Kumar; Rupp, Richard Helmut; De Souza, Noel John
PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 9 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| DE 3624702 | A1 | 19880204 | DE 1986-3624702 | 19860722 | <-- |
| IN 164921 | A1 | 19890708 | IN 1986-BO149 | 19860515 | <-- |
| EP 254224 | A2 | 19880127 | EP 1987-110365 | 19870717 | <-- |
| EP 254224 | A3 | 19890419 | | | |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | | |
| ZA 8705297 | A | 19880330 | ZA 1987-5297 | 19870720 | <-- |
| US 4803204 | A | 19890207 | US 1987-75643 | 19870720 | <-- |
| DK 8703802 | A | 19880123 | DK 1987-3802 | 19870721 | <-- |
| JP 63033365 | A | 19880213 | JP 1987-180207 | 19870721 | <-- |
| HU 44516 | A2 | 19880328 | HU 1987-3360 | 19870721 | <-- |
| AT 8702609 | A | 19881215 | AT 1987-2609 | 19871008 | <-- |
| AT 388553 | B | 19890725 | | | |
| PRIORITY APPLN. INFO.: | | | DE 1986-3624702 | A 19860722 | |
| OTHER SOURCE(S): | | MARPAT 109:73142 | | | |

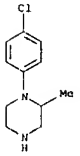
GI







AB The title compds. I [R1,R3 = H, alkyl, carbalkoxy, Ph (un)substituted with alkyl, halo, or NH2; R2 = halo, CF3; n = 0-3; X = O, N; when X = O, R4 = alkyl; when X = N, XR4 = dialkylamino, 5- or 6-membered heterocyclyl optionally containing another heteroatom, optionally substituted with (un)substituted alkyl or Ph (un)substituted with alkyl, alkoxy, or halo], having high activity against the pathogens of malaria and coccidiosis, were prepared A suspension of 7-chloro-3,4-dihydro-10-hydroxy-3-(4-trifluoromethylphenyl)-1,9(2H,10H)-acridinedione in MeOH was treated dropwise with pyrrolidine at room temperature to give 78% I [R1 = R3 = H, (R2)n = 4-CF3, XR4 = pyrrolidine]. At 10-25 mg I/ kg + S in mice infected with Plasmodium berghei, complete healing was achieved.
IT 55117-80-1, 1-(4-Chlorophenyl)-2-methylpiperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(aminolysis by, of hydroxyacridinedione derivative)
RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)

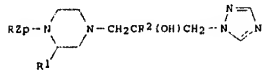


L9 ANSWER 68 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:620995 CAPLUS
DOCUMENT NUMBER: 105:220995
TITLE: Piperazinylmethyl-1,2,4-triazolylmethylcarbinol fungicide
INVENTOR(S): Holmwood, Graham; Buechel, Karl Heinz; Brandes, Wilhelm; Reinecke, Paul
PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 44 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 3508909 | A1 | 19860918 | DE 1985-3508909 | 19850313 <-- |
| US 4738962 | A | 19880419 | US 1986-832502 | 19860221 <-- |
| EP 198191 | A1 | 19861022 | EP 1986-102767 | 19860303 <-- |
| EP 198191 | B1 | 19890906 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE | | | | |
| AT 46152 | T | 19890915 | AT 1986-102767 | 19860303 <-- |
| AU 8654433 | A | 19861016 | AU 1986-54433 | 19860307 <-- |
| JP 61212568 | A | 19860920 | JP 1986-51578 | 19860311 <-- |
| DD 243848 | A5 | 19870318 | DD 1986-287770 | 19860311 <-- |
| DK 8601144 | A | 19860914 | DK 1986-1144 | 19860312 <-- |
| BR 8601052 | A | 19861125 | BR 1986-1052 | 19860312 <-- |
| ZA 8601843 | A | 19861126 | ZA 1986-1843 | 19860312 <-- |
| HU 42280 | A2 | 19870728 | HU 1986-1060 | 19860313 <-- |
| ES 552966 | A1 | 19871101 | ES 1986-552966 | 19860313 <-- |
| PRIORITY APPLN. INFO.: | | | DE 1985-3508909 A | 19850313 |
| | | | EP 1986-102767 A | 19860303 |

OTHER SOURCE(S): CASREACT 105:220995

GI



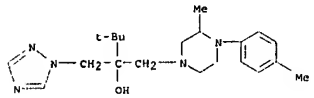
I

AB The title compds. I (R = substituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, aryloxyalkyl, arylthioalkyl; R1 = H, alkyl; R2 = substituted alkyl, alkenyl, cycloalkyl, aryl heterocyclyl; Z = CO, SO2; p = 0,or 1) are prepared as agricultural and medical fungicides. Thus, 16.7 g 2-tert-butyl-1-(1,2,4-triazol-1-yl)methyloxirane, 16.2 g 1-phenylpiperazine and 150 mL EtOH was refluxed for 15 h to give 19 g 3,3-dimethyl-2-[1-(4-phenylpiperazin-1-yl)-methyl]-1-(1,2,4-triazol-1-yl)buten-2-ol. I are active against Pyrenophora teres on barley and Uromyces appendiculatus on bean. I are also medical virucides.

IT 105411-76-5P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as fungicide)

RN 105411-76-5 CAPLUS

CN 1-Piperazineethanol, α-(1,1-dimethylethyl)-3-methyl-4-(4-methylphenyl)-α-(1H-1,2,4-triazol-1-ylmethyl)- (9CI) (CA INDEX NAME)







L9 ANSWER 69 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:566904 CAPLUS
DOCUMENT NUMBER: 105:166904
TITLE: Herbicide antidote
INVENTOR(S): Foery, Werner; Nyffeler, Andreas; Gerber, Hans Rudolf; Martin, Henry
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
SOURCE: Eur. Pat. Appl., 143 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 190105 | A2 | 19860806 | EP 1986-810046 | 19860127 <-- |
| EP 190105 | A3 | 19881026 | | |
| R: BE, CH, DE, FR, GB, IT, LI, NL | | | | |
| CA 1278695 | C | 19910108 | CA 1986-500569 | 19860129 <-- |
| BR 8600383 | A | 19861014 | BR 1986-383 | 19860130 <-- |
| JP 61176504 | A | 19860808 | JP 1986-20005 | 19860131 <-- |
| PRIORITY APPLN. INFO.: | | | CH 1985-418 A | 19850131 |

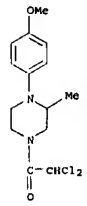
OTHER SOURCE(S): MARPAT 105:166904

AB The dichloroacetamides RR1NCOCHCl2 (R,R1 = H, (un)substituted alkyl, alkenyl, cycloalkyl, cycloalkenyl, etc.; NRR1 = heterocyclic radical) are prepared as antidotes for the N-(2-methoxycarbonylphenylsulfonyl)-N-(4,6-bisdifluoromethoxypyrimidin-2-yl)urea (I) herbicide. Thus, condensation of N-(3,4-dimethoxybenzyl)-N-isopropylamine (preparation given) with Cl2CHCOCl, in NaOH-containing MePh, at -10 to -15°, gave N-(3,4-dimethoxybenzyl)-N-iso-Pr dichloroacetanilide. When (H2C:CHCH2)2NCOCHCl2 (200 g/ha) was applied to corn in tank mixture with 400 g I/ha, 75% protection against the phytotoxicity of I to the crop was observed

IT 104767-29-5P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antidote for sulfonylurea herbicide)

RN 104767-29-5 CAPLUS

CN Piperazine, 4-(dichloroacetyl)-1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)







L9 ANSWER 70 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:132069 CAPLUS
DOCUMENT NUMBER: 102:132069
TITLE: [[4-[4-(4-Phenyl-1-piperazinyl)phenoxymethyl]-1,3-dioxolan-2-yl]methyl]-1H-imidazoles and 1H-1,2,4-triazoles
INVENTOR(S): Heeres, Jan; Stokbroekx, Raymond A.; Backx, Leo J. J.
PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.
SOURCE: Eur. Pat. Appl., 113 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 118138 | A1 | 19840912 | EP 1984-200092 | 19840124 <-- |
| EP 118138 | B1 | 19890614 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| US 4619931 | A | 19861028 | US 1984-569122 | 19840109 <-- |
| AT 44030 | T | 19890615 | AT 1984-200092 | 19840124 <-- |
| CA 1271194 | A1 | 19900703 | CA 1984-447194 | 19840210 <-- |
| JP 59172486 | A | 19840929 | JP 1984-32768 | 19840224 <-- |
| JP 07042285 | B | 19950510 | | |
| DK 8401070 | A | 19840829 | DK 1984-1070 | 19840227 <-- |
| DK 164454 | B | 19920629 | | |
| DK 164454 | C | 19921109 | | |
| FI 8400781 | A | 19840829 | FI 1984-781 | 19840227 <-- |
| FI 82043 | B | 19900928 | | |
| FI 82043 | C | 19910110 | | |
| NO 8400735 | A | 19840829 | NO 1984-735 | 19840227 <-- |
| NO 160138 | B | 19881205 | | |
| NO 160138 | C | 19890315 | | |
| AU 8425097 | A | 19840906 | AU 1984-25097 | 19840227 <-- |
| AU 559461 | B2 | 19870312 | | |
| ZA 8401449 | A | 19851030 | ZA 1984-1449 | 19840227 <-- |
| IL 71066 | A | 19871220 | IL 1984-71066 | 19840227 <-- |
| ES 530138 | A1 | 19850516 | ES 1984-530138 | 19840228 <-- |
| ES 530140 | A1 | 19850601 | ES 1984-530140 | 19840228 <-- |
| ES 530139 | A1 | 19850901 | ES 1984-530139 | 19840228 <-- |
| US 4735942 | A | 19880405 | US 1986-869537 | 19860602 <-- |
| NO 8702221 | A | 19840829 | NO 1987-2221 | 19870527 <-- |
| NO 163817 | B | 19900417 | | |
| NO 163817 | C | 19900725 | | |
| US 4861879 | A | 19890829 | US 1988-154173 | 19880209 <-- |
| CA 1309412 | C2 | 19921027 | CA 1989-615528 | 19891025 <-- |
| FI 84058 | B | 19910628 | FI 1989-5089 | 19891026 <-- |
| FI 84058 | C | 19911010 | | |
| NO 9000396 | A | 19840829 | NO 1990-396 | 19900129 <-- |
| NO 173866 | B | 19931108 | | |
| NO 173866 | C | 19940216 | | |
| JP 05246999 | A | 19930924 | JP 1991-24132 | 19910124 <-- |
| JP 07064823 | B | 19950712 | | |
| DK 9100783 | A | 19910429 | DK 1991-783 | 19910429 <-- |
| DK 9101088 | A | 19910607 | DK 1991-1088 | 19910607 <-- |
| DK 166673 | B1 | 19930628 | | |
| PRIORITY APPLN. INFO.: | | | US 1983-470405 A | 19830228 |





| | | | |
|---|---|---|---|
| | US 1984-569122 | A | 19840109 |
| | EP 1984-200092 | A | 19840124 |
| | CA 1984-447194 | A3 | 19840210 |
| | FI 1984-781 | A | 19840227 |
| | NO 1984-735 | A1 | 19840227 |
| | US 1986-869537 | A3 | 19860602 |

OTHER SOURCE(S): CASREACT 102:132069; MARPAT 102:132069

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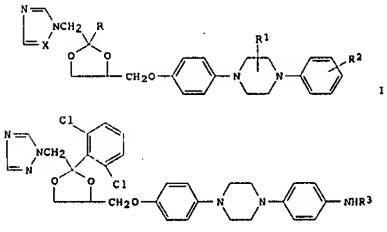


I



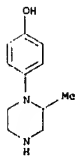
II

AB Over 300 title compds. I [R = (un)substituted Ph; R1 = H, alkyl; R2 = urea, thiourea, amido, 5-membered N-containing heterocycle; X = N, CH] and their intermediates, useful as pharmaceutical fungicides, were prepared Thus, aniline derivative II (R3 = H) was treated with ClCO2Ph to give II (R3 = CO2Ph). At 2.5 mg/kg orally, daily for 3 days in rats, II (R3 = CO2Ph) controlled Candida albicans at the 14th day after infection.

IT 95182-89-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation of)

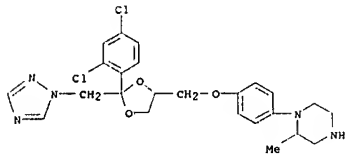
RN 95182-89-1 CAPLUS

CN Phenol, 4-(2-methyl-1-piperazinyl)-, dihydrobromide (9CI) (CA INDEX NAME)



●2 HBr

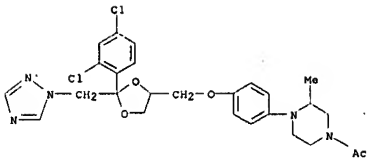
IT 95182-92-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and arylation of)
RN 95182-92-6 CAPLUS
CN Piperazine, 1-[4-[[2-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-2-methyl- (9CI) (CA INDEX NAME)



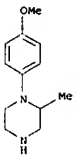
IT 95182-91-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deacylation of)
RN 95182-91-5 CAPLUS
CN Piperazine, 4-acetyl-1-[4-[[2-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-2-methyl- (9CI) (CA INDEX NAME)



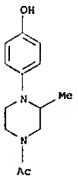




IT 35947-12-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)
RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



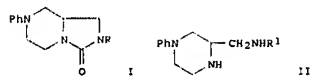
IT 95182-90-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with dioxolanemethanol derivative)
RN 95182-90-4 CAPLUS
CN Piperazine, 4-acetyl-1-(4-hydroxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



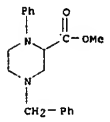




L9 ANSWER 71 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:490876 CAPLUS
DOCUMENT NUMBER: 101:90876
TITLE: Hexahydroimidazo[1,5-a]pyrazines. II. Synthesis of 7-phenyl-1,5,6,7,8,8a-hexahydroimidazo[1,5-a]pyrazin-3(2H)-one and derivatives
AUTHOR(S): Toja, E.; Omodei-Sale, A.; Corsico, N.
CORPORATE SOURCE: Lab. Ric., Gruppo Lepetit S.p.A., Milan, Italy
SOURCE: Farmaco, Edizione Scientifica (1984), 39(5), 450-62
CODEN: FRPSAX; ISSN: 0430-0920
DOCUMENT TYPE: Journal
LANGUAGE: Italian
OTHER SOURCE(S): CASREACT 101:90876
GI



AB Title compds. I (R = Ph, tolyl, ClC6H4, anisyl, Me, allyl), useful as central nervous system depressants, were prepared from piperazines II (R1 = Ph, tolyl, ClC6H4 anisyl, H). A mixture of II (R1 = H) and 1,1'-carbonyldiimidazole in THF was kept 11 days at room temperature, and the product was treated with NaH and MeI in DMF to give I (R = Me).
IT 91532-79-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 91532-79-5 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-4-(phenylmethyl)-, methyl ester (9CI) (CA INDEX NAME)

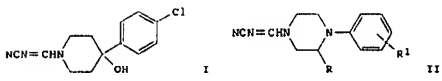


L9 ANSWER 72 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:490874 CAPLUS
DOCUMENT NUMBER: 101:90874
TITLE: Antimycotic agents, XVI. Halogenated (cyanaminomethylene)piperidines and -piperazines
AUTHOR(S): Kreutzberger, Alfred; Kreutzberger, Elfriede
CORPORATE SOURCE: Inst. Pharm., Johannes Gutenberg-Univ., Mainz, 6500,

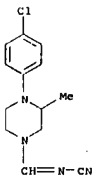




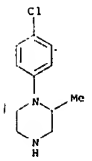
Fed. Rep. Ger.
SOURCE: Archiv der Pharmazie (Weinheim, Germany) (1984), 317(5), 417-20
CODEN: ARPMAS; ISSN: 0365-6233
DOCUMENT TYPE: Journal
LANGUAGE: German
GI



AB Aminomethylating H2NCN with s-trazine in the presence of secondary amines gave cyanomethylene heterocycles I and II [R = Me, R1 = p-Cl; R = H, R1 = p-F, m-F3C, 4,3-Cl(F3C)], classed as dehydro-N-Mannich bases. I and II [R1 = 4,3-Cl(F3C)] showed antimycotic activity (no data).
IT 91126-05-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 91126-05-5 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-4-[(cyanoimino)methyl]-2-methyl- (9CI) (CA INDEX NAME)



IT 55117-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with cyanamide and triazine)
RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 73 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:423499 CAPLUS
DOCUMENT NUMBER: 101:23499
TITLE: Piperazine derivatives with anticholinergic and antihistaminic activity
INVENTOR(S): Milani, Carlo; Carminati, Giovanni Maria; Sovera, Attilio
PATENT ASSIGNEE(S): Selvi e C. S.p.A., Italy
SOURCE: Belg., 49 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: Dutch
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| BE 897828 | A2 | 19840116 | BE 1983-60212 | 19830927 | <-- |
| US 4457931 | A | 19840703 | US 1982-424512 | 19820927 | <-- |
| ZA 8306949 | A | 19840530 | ZA 1983-6949 | 19830919 | <-- |
| JP 59089665 | A | 19840523 | JP 1983-176190 | 19830922 | <-- |
| JP 61039289 | B | 19860903 | | | |
| FR 2533564 | A1 | 19840330 | FR 1983-15172 | 19830923 | <-- |
| FR 2533564 | B1 | 19861003 | | | |
| DE 3334757 | A1 | 19840329 | DE 1983-3334757 | 19830926 | <-- |
| ES 525953 | A1 | 19860201 | ES 1983-525953 | 19830926 | <-- |
| AT 8303412 | A | 19880915 | AT 1983-3412 | 19830926 | <-- |
| AT 387964 | B | 19890410 | | | |
| NL 8303311 | A | 19840416 | NL 1983-3311 | 19830927 | <-- |
| GB 2135991 | A | 19840912 | GB 1983-25839 | 19830927 | <-- |
| GB 2135991 | B | 19851204 | | | |
| ES 542946 | A1 | 19860101 | ES 1985-542946 | 19850416 | <-- |
| ES 542947 | A1 | 19860101 | ES 1985-542947 | 19850416 | <-- |

PRIORITY APPLN. INFO.: US 1982-424512 A 19820927
OTHER SOURCE(S): CASREACT 101:23499; MARPAT 101:23499
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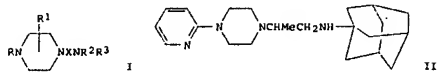


I II



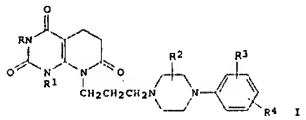


IT 2946-76-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with chloroethylmorpholine)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

L9 ANSWER 74 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:407184 CAPLUS
DOCUMENT NUMBER: 101:7184
TITLE: Pyridopyrimidinetriones, their use, and drugs containing them
INVENTOR(S): Klemm, Kurt; Pruesse, Wolfgang; Baron, Lothar; Kilian, Ulrich; Sanders, Karl
PATENT ASSIGNEE(S): Byk-Gulden Lomberg Chemische Fabrik G.m.b.H., Fed. Rep. Ger.
SOURCE: Ger. Offen., 50 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| DE 3326118 | A1 | 19840209 | DE 1983-3326118 | 19830720 | <-- |

PRIORITY APPLN. INFO.: CH 1982-4651 A 19820802
OTHER SOURCE(S): MARPAT 101:7184
GI



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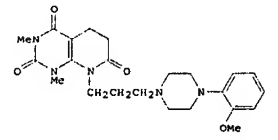
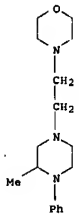


II

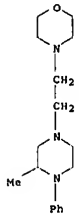




AB Aminoalkylpiperazines I (X = alkylene; R = aryl, aralkyl, heterocyclic; R1 = H, alkyl; R2, R3 = H, alkyl, cycloalkyl, aryl; NR2R3 = heterocyclic) were prepared Thus, 1-(2-pyridyl)piperazine was treated with BrCHMeCH2CO2Et and the resulting ester reduced to the alc., brominated, and aminated with 1-adamantylamine to give II. II had an anticholinergic ED50 in vitro of 0.001 μg/mL.
IT 90476-58-7P 90476-80-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and anticholinergic and antihistaminic activity of)
RN 90476-58-7 CAPLUS
CN Morpholine, 4-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 90476-80-5 CAPLUS
CN Morpholine, 4-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]-, trihydrochloride (9CI) (CA INDEX NAME)

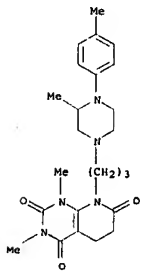


●3 HCl

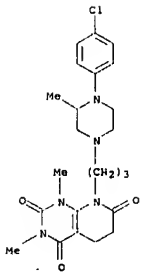




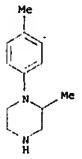
AB Title compds. (I) (R = H, C1-5 alkyl; R1 = C1-5 alkyl; R2 = H, C1-3 alkyl; R3 = H, halo, C1-4 alkyl or alkoxy, CF3; R4 = H, halo, C1-4 alkyl or alkoxy) and their N-oxides and salts were prepared and shown to have antihypertensive activity. Thus, 6-[[3-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]amino]-1,3-dimethyluracil was added to CH2:CHCO2Et, and the product saponified, then cyclized by heating 1 h at 140°/12-15 mbar to give the pyridopyrimidinetrione II.
IT 89989-10-6P 89989-11-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antihypertensive)
RN 89989-10-6 CAPLUS
CN Pyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione, 5,8-dihydro-1,3-dimethyl-8-[3-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)



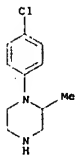
RN 89989-11-7 CAPLUS
CN Pyrido[2,3-d]pyrimidine-2,4,7(1H,3H,6H)-trione, 8-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]propyl]-5,8-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



IT 35947-11-6 55117-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (chloropropyl)pyridopyrimidinetrione derivs.)
RN 35947-11-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)- (CA INDEX NAME)



RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



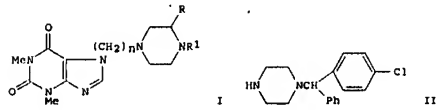




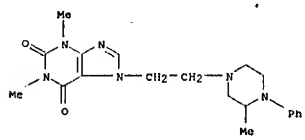
L9 ANSWER 75 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:85510 CAPLUS
DOCUMENT NUMBER: 100:85510
TITLE: Theophylline derivatives as cerebral circulation improvers
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 58150511 | A | 19830907 | JP 1982-31686 | 19820302 <-- |
| PRIORITY APPLN. INFO.: | | | JP 1982-31686 | 19820302 |

GI



AB Ninety-five theophyllines I (R = H, Me; R1 = aryl, Ph2CH, pyridyl; n = 2-10) were prepared and were effective cerebral vasodilators at 0.1-10 μg/kg. Thus, refluxing 7-(2-bromoethyl)theophylline 6.3, piperazine II 5.7, and Et3N 4.0 g in C6H6 18.5 h gave 42.5% I.HCl (R = H, R1 = p-chlorobenzhydryl, n = 2).
IT 81996-76-1P 81996-77-2P 81996-78-3P
81996-79-4P 81996-80-7P 81996-84-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 81996-76-1 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

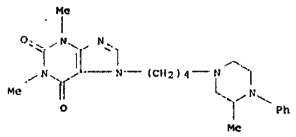


RN 81996-77-2 CAPLUS

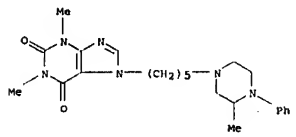




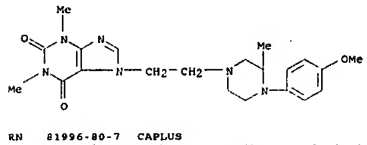
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[4-(3-methyl-4-phenyl-1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)



RN 81996-78-3 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[5-(3-methyl-4-phenyl-1-piperazinyl)pentyl]- (9CI) (CA INDEX NAME)



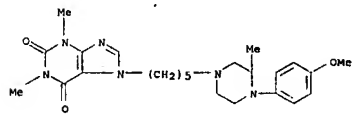
RN 81996-79-4 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)



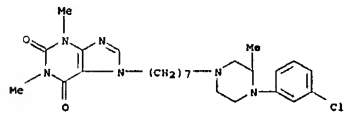
RN 81996-80-7 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[5-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]pentyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)







RN 81996-84-1 CAPLUS
CN 1H-Purine-2,6-dione, 7-[7-[4-(3-chlorophenyl)-3-methyl-1-piperazinyl]heptyl]-3,7-dihydro-1,3-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)

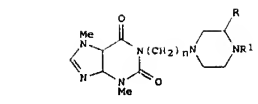


● HCl

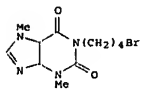
L9 ANSWER 76 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:68315 CAPLUS
DOCUMENT NUMBER: 100:68315
TITLE: Theobromine derivatives as brain circulation improvers
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 58148820 | A | 19830905 | JP 1982-29043 | 19820226 <-- |
| PRIORITY APPLN. INFO.: | | | JP 1982-29043 | 19820226 |

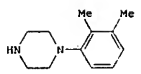
GI



I



II



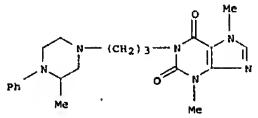
III

AB Fifty-five theobromine derivs. (I; R = H, alkyl; R1 = aryl, benzhydryl; n = 2-10) and their acid adducts, effective brain circulation improvers at 0.1-10 μg/kg, were prepared Thus, a mixture of theobromine derivative II 9.5, piperazine derivative III 3.8, and Et3N 4.0 g in MePh was refluxed 13 h to give 41.6% I (R = H, R1 = 2,3-xylyl, n = 4).

IT 81995-72-4P 81995-73-5P 81995-74-6P
81995-75-7P 81995-76-8P 81995-77-9P
81995-78-0P 81997-11-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

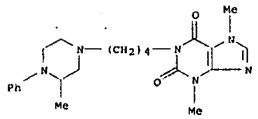
RN 81995-72-4 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[3-(3-methyl-4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



RN 81995-73-5 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[4-(3-methyl-4-phenyl-1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)

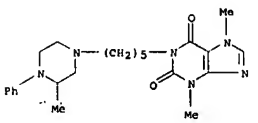






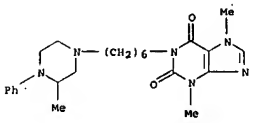
RN 81995-74-6 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[5-(3-methyl-4-phenyl-1-piperazinyl)pentyl]- (9CI) (CA INDEX NAME)



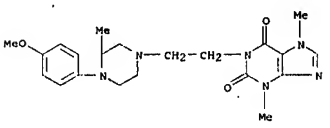
RN 81995-75-7 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[6-(3-methyl-4-phenyl-1-piperazinyl)hexyl]- (9CI) (CA INDEX NAME)



RN 81995-76-8 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)

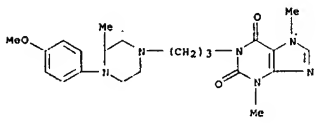


RN 81995-77-9 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)

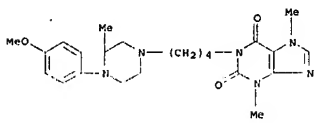






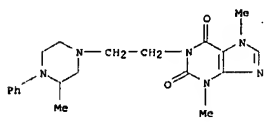
RN 81995-78-0 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[4-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]butyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



RN 81997-11-7 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 77 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1983:600512 CAPLUS

DOCUMENT NUMBER: 99:200512

TITLE: Composition for the treatment of pain, fever, tissue and/or bone and joint inflammation, containing theobromine or theophylline derivatives as active constituents

INVENTOR(S): Kaneko, Takeru; Ozaki, Satoru; Takizawa, Kimie; Sugimoto, Hachiro

PATENT ASSIGNEE(S): Eisai Co., Ltd. , Japan

SOURCE: Ger. Offen., 80 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1





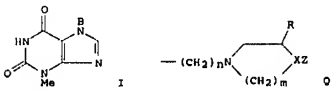
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 3307395 | A1 | 19830908 | DE 1983-3307395 | 19830302 <-- |
| JP 58148818 | A | 19830905 | JP 1982-31684 | 19820302 <-- |
| JP 01018050 | B | 19890403 | | |
| JP 58148819 | A | 19830905 | JP 1982-31685 | 19820302 <-- |
| JP 01013689 | B | 19890307 | | |
| EP 87810 | A1 | 19830907 | EP 1983-102019 | 19830302 <-- |
| EP 87810 | B1 | 19860625 | | |
| R: BE, CH, DE, FR, GB, IT, LI, NL, SE | | | | |
| US 4543254 | A | 19850924 | US 1983-471564 | 19830302 <-- |
| US 4599337 | A | 19860708 | US 1985-755404 | 19850716 <-- |

PRIORITY APPLN. INFO.: JP 1982-31684 A 19820302
JP 1982-31685 A 19820302
US 1983-471564 A3 19830302

OTHER SOURCE(S): CASREACT 99:200512; MARPAT 99:200512

GI

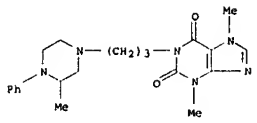


AB I, in which one of A and B is Me and the other is Q (R is H or lower alkyl; Z is C6H3X1X2 [X1 and X2 are H, lower alkyl or alkoxy, F3C, or halogen], pyridyl, or CH(C6H4Y1)(C6H4Y2) [Y1 and Y2 are H, lower alkyl or alkoxy, F3C, or halogen]; X is N or C, m is 2 or 3, and n is 2-10) are analgesics, antipyretics, and inflammation inhibitors. Analgesic activity (ED50), LD50, and LD50/ED50 ratio values of representative compds. in mice and rats, antipyretic, and antiphlogistic activities are reported. Thus, 7-(2-bromoethyl)theophylline [23146-05-6] and 1-(p-chlorobenzhydryl)piperazine [303-26-4] were refluxed with Et3N in C6H6, the Et3N.HCl obtained was filtered, the filtrate was extracted with dilute HCl, made alkaline and extracted with CHCl3. The extract was washed, dried, evaporated, and the crystals were converted to the HCl salt and recrystd. from Me Cellosolve-H2O to obtain 7-[2-[4-(p-chlorobenzhydryl)piperazinyl]ethyl]theophylline-2HCl [82013-70-5]. Formulation of tablets and capsules with typical excipients is described.

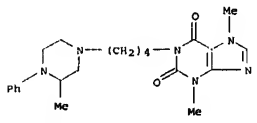
IT 81995-72-4P 81995-73-5P 81995-74-6P
81995-75-7P 81995-76-8P 81995-77-9P
81995-78-0P 81996-76-1P 81996-77-2P
81996-79-4P 81996-80-7P 81996-84-1P
81997-11-7P 87798-78-5P
RL: THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, for analgesics and antipyretics and inflammation inhibitors)

RN 81995-72-4 CAPLUS

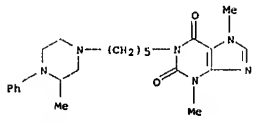
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[3-(3-methyl-4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



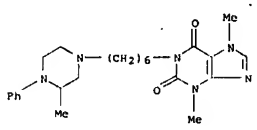
RN 81995-73-5 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[4-(3-methyl-4-phenyl-1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)



RN 81995-74-6 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[5-(3-methyl-4-phenyl-1-piperazinyl)pentyl]- (9CI) (CA INDEX NAME)



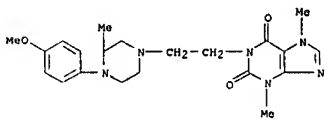
RN 81995-75-7 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[6-(3-methyl-4-phenyl-1-piperazinyl)hexyl]- (9CI) (CA INDEX NAME)



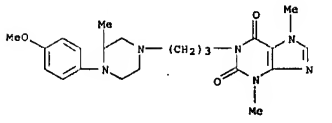




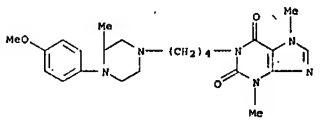
RN 81995-76-8 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



RN 81995-77-9 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



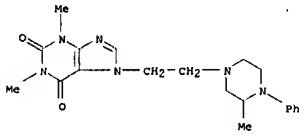
RN 81995-78-0 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[4-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]butyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



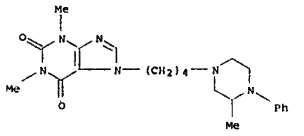
RN 81996-76-1 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



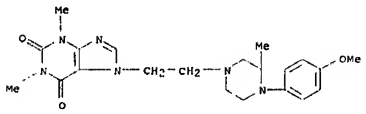




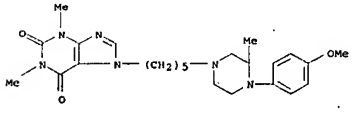
RN 81996-77-2 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[4-(3-methyl-4-phenyl-1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)



RN 81996-79-4 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)



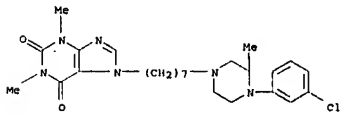
RN 81996-80-7 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[5-(4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]pentyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)





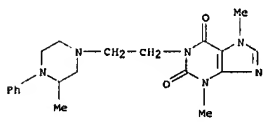


RN 81996-84-1 CAPLUS
CN 1H-Purine-2,6-dione, 7-[7-[4-(3-chlorophenyl)-3-methyl-1-piperazinyl]heptyl]-3,7-dihydro-1,3-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)

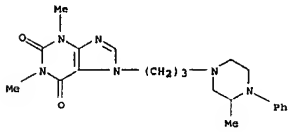


● HCl

RN 81997-11-7 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



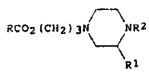
RN 87798-78-5 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[3-(3-methyl-4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 78 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:470678 CAPLUS
DOCUMENT NUMBER: 99:70678
TITLE: Chemistry of 1,3-bifunctional compounds. XXVII. Preparation of 4-*N*-substituted piperazinyl-1-propyl

esters

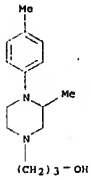
AUTHOR(S): Felfoldi, K.; Molnar, A.; Apjok, J.; Czombos, J.; Notheisz, F.; Karpati, E.
CORPORATE SOURCE: Dep. Org. Chem., Jozsef Attila Univ., Szeged, 6720, Hung.
SOURCE: Acta Physica et Chemica (1982), 28(3-4), 225-44
CODEN: AUSHAF; ISSN: 0001-6721
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 99:70678
GI



I

AB N-Piperazinepropanol esters I [R = Ph, methoxy-, halo-, or methylphenyl, xanthenyl, methoxycyclohexyl, furyl; R1 = H, Me; R2 = alkyl, alkenyl, cyclohexylmethyl, phenylalkyl, PhOCH2CH2, CO2Et, PhCH:CHCH2, 2,6-Me2C6H3NHCOCH2, Ph, tolyl, Me2C6H3, anisyl, chlorophenyl, F3CC6H4, pyridyl, (un)substituted benzyl] were prepared Some of the above products exhibited antiarrhythmic activity. Thus, 1-(3-hydroxypropyl)-4-isopropylpiperazine was treated with 3-MeOC6H4COCl to give I (R = 3-MeOC6H4, R1 = H, R2 = CHMe2).

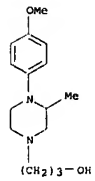
IT 86571-52-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and esterification by, of acid chlorides)
RN 86571-52-0 CAPLUS
CN 1-Piperazinepropanol, 3-methyl-4-(4-methylphenyl)- (9CI) (CA INDEX NAME)



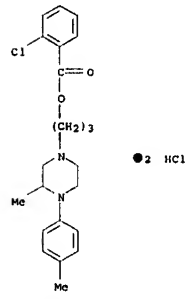
IT 86571-53-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and esterification by, of benzoyl chlorides)
RN 86571-53-1 CAPLUS
CN 1-Piperazinepropanol, 4-(4-methoxyphenyl)-3-methyl- (9CI) (CA INDEX NAME)







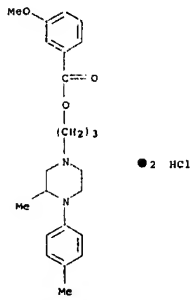
IT 86571-88-2P 86571-89-3P 86571-90-6P
86572-02-3P 86572-03-4P 86585-77-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 86571-88-2 CAPLUS
CN Benzoic acid, 2-chloro-, 3-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]propyl ester, dihydrochloride (9CI) (CA INDEX NAME)



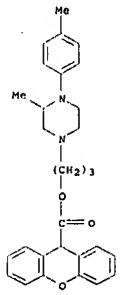
RN 86571-89-3 CAPLUS
CN Benzoic acid, 3-methoxy-, 3-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]propyl ester, dihydrochloride (9CI) (CA INDEX NAME)







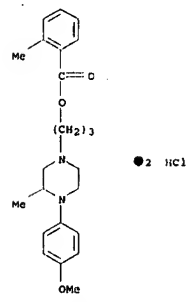
RN 86571-90-6 CAPLUS
CN 9H-Xanthene-9-carboxylic acid, 3-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]propyl ester, dihydrochloride (9CI) (CA INDEX NAME)



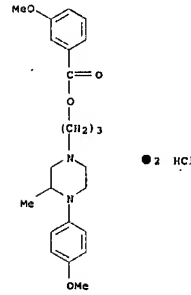
RN 86572-02-3 CAPLUS
CN Benzoic acid, 2-methyl-, 3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propyl ester, dihydrochloride (9CI) (CA INDEX NAME)



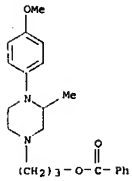




RN 86572-03-4 CAPLUS
CN Benzoic acid, 3-methoxy-, 3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propyl ester, dihydrochloride (9CI) (CA INDEX NAME)

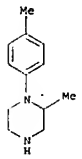


RN 86585-77-5 CAPLUS
CN 1-Piperazinepropanol, 4-(4-methoxyphenyl)-3-methyl-, benzoate (ester), dihydrochloride (9CI) (CA INDEX NAME)

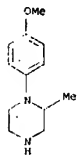


●2 HCl

IT 35947-11-6 35947-12-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-alkylation of, by chloropropanol)
RN 35947-11-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)- (CA INDEX NAME)



RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)





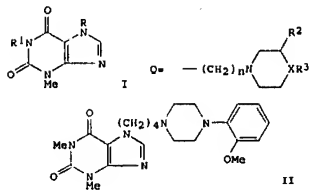


L9 ANSWER 79 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1982:438769 CAPLUS
DOCUMENT NUMBER: 97:38769
TITLE: Derivatives of theophylline and theobromine
PATENT ASSIGNEE(S): Eisai Co., Ltd. , Japan
SOURCE: Belg., 59 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| BE 890222 | A1 | 19820104 | BE 1981-59339 | 19810904 <-- |
| JP 57046983 | A | 19820317 | JP 1980-121712 | 19800904 <-- |
| JP 57046984 | A | 19820317 | JP 1980-121713 | 19800904 <-- |
| JP 63060756 | B | 19881125 | | |
| US 4426383 | A | 19840117 | US 1981-298227 | 19810831 <-- |
| NL 8104073 | A | 19820401 | NL 1981-4073 | 19810902 <-- |
| SE 8105240 | A | 19820305 | SE 1981-5240 | 19810903 <-- |
| SE 456910 | B | 19881114 | | |
| SE 456910 | C | 19890309 | | |
| GB 2083470 | A | 19820324 | GB 1981-26653 | 19810903 <-- |
| GB 2083470 | B | 19840912 | | |
| DE 3134929 | A1 | 19820609 | DE 1981-3134929 | 19810903 <-- |
| CA 1172632 | A1 | 19840814 | CA 1981-385142 | 19810903 <-- |
| CH 651042 | A5 | 19850830 | CH 1981-5675 | 19810903 <-- |
| FR 2489331 | A1 | 19820305 | FR 1981-16855 | 19810904 <-- |
| FR 2489331 | B1 | 19841130 | | |
| US 4564617 | A | 19860114 | US 1983-484044 | 19830411 <-- |
| SE 8704599 | A | 19871120 | SE 1987-4599 | 19871120 <-- |
| SE 457083 | B | 19881128 | | |
| SE 457083 | C | 19890323 | | |

PRIORITY APPLN. INFO.:
JP 1980-121712 A 19800904
JP 1980-121713 A 19800904
US 1981-298227 A3 19810831

OTHER SOURCE(S): CASREACT 97:38769; MARPAT 97:38769
GI



I

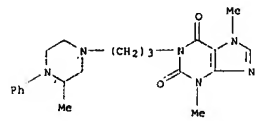


II

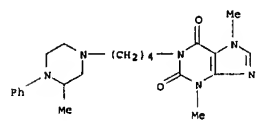




AB The title derivs. I [R, R1 = Me, Q [R2 = H, alkyl; R3 = (un)substituted Ph, (un)substituted diphenylmethyl; X = N, CH; n = 2-10]] were prepared Thus, 7-(4-bromobutyl)theophylline was treated with 1-(o-methoxyphenyl)piperazine to give 37.6% theophylline II. At 0.1 μg/kg the vasodilator II.2 HCl increased the arterial blood flow. I also had central nervous system, antihistaminic, analgesic, antihypertensive, and antiasthmatic activity (no data).
IT 81995-72-4P 81995-73-5P 81995-74-6P
81995-75-7P 81995-76-8P 81995-77-9P
81995-78-0P 81996-76-1P 81996-77-2P
81996-78-3P 81996-79-4P 81996-80-7P
81996-84-1P 81997-11-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 81995-72-4 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[3-(3-methyl-4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



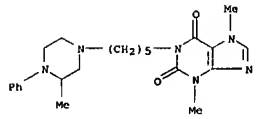
RN 81995-73-5 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[4-(3-methyl-4-phenyl-1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)



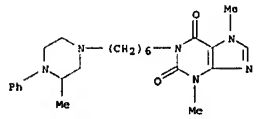
RN 81995-74-6 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[5-(3-methyl-4-phenyl-1-piperazinyl)pentyl]- (9CI) (CA INDEX NAME)



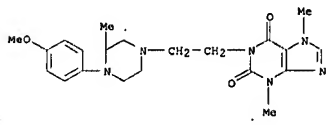




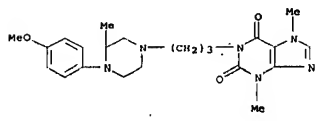
RN 81995-75-7 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[6-(3-methyl-4-phenyl-1-piperazinyl)hexyl]- (9CI) (CA INDEX NAME)



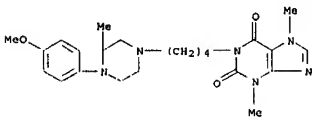
RN 81995-76-8 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



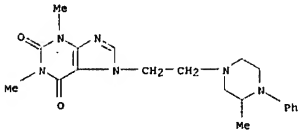
RN 81995-77-9 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



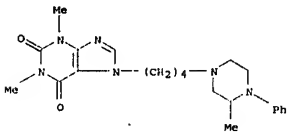
RN 81995-78-0 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-[4-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]butyl]-3,7-dimethyl- (9CI) (CA INDEX NAME)



RN 81996-76-1 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



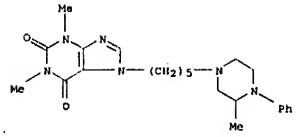
RN 81996-77-2 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[4-(3-methyl-4-phenyl-1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)



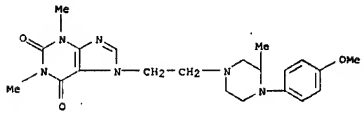
RN 81996-78-3 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[5-(3-methyl-4-phenyl-1-piperazinyl]pentyl]- (9CI) (CA INDEX NAME)



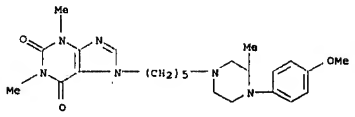




RN 81996-79-4 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)



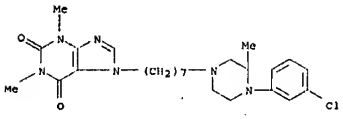
RN 81996-80-7 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[5-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]pentyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 81996-84-1 CAPLUS
CN 1H-Purine-2,6-dione, 7-[7-[4-(3-chlorophenyl)-3-methyl-1-piperazinyl]heptyl]-3,7-dihydro-1,3-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)

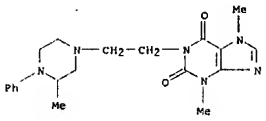




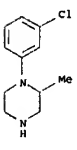


● HCl

RN 81997-11-7 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



IT 75348-33-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (haloalkyl)theophylline)
RN 75348-33-3 CAPLUS
CN Piperazine, 1-(3-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)

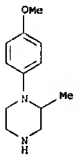


IT 2946-76-1 35947-12-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (haloalkyl)theophylline and (bromoalkyl)theobromine)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)





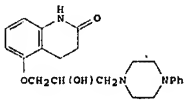
RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 80 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:491203 CAPLUS
DOCUMENT NUMBER: 95:91203
TITLE: Central nervous system depressants
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 48 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 55046812 | A | 19810428 | JP 1979-124878 | 19790927 <-- |
| JP 02012204 | B | 19900319 | | |

PRIORITY APPLN. INFO.: JP 1979-124878 A 19790927
GI



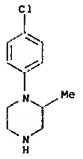
● HCl

I

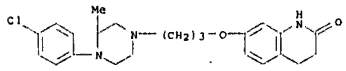
AB 5-[2-Hydroxy-3-(4-phenylpiperazinyl)propoxy]-3,4-dihydrocarbostyril-HCl (I) [72566-28-0] and its analogs are central nervous system depressants.

Thus, I and its analogs increased the anesthetic effect of halothane in mice. I was synthesized by treating 5-(2,3-epoxypropoxy)-3,4-dihydrocarbostyril [51781-14-7] with 4-phenylpiperazine [92-54-6]. Similarly, .apprx.130 analogs were synthesized.

IT 55117-80-1
RL: BIOL (Biological study)
(condensation of, with (chloropropoxy)dihydrocarbostyril)
RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



IT 76808-65-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 76808-65-6 CAPLUS
CN 2(1H)-Quinolinone, 7-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]propoxy]-3,4-dihydro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L9 ANSWER 81 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:425127 CAPLUS
DOCUMENT NUMBER: 95:25127
TITLE: Carbostyril derivatives
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 32 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

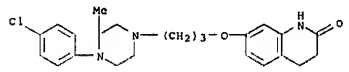
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|





| | | | | | |
|---|---|---|---|---|---|
| JP 55162774 | A | 19801218 | JP 1979-71434 | | 19790606 <-- |
| PRIORITY APPLN. INFO.: | | | JP 1979-71434 | A | 19790606 |

OTHER SOURCE(S): CASREACT 95:25127
GI For diagram(s), see printed CA Issue.
AB Forty-seven carbostyrils I [R = H, Q (R6 = H, OH, alkyl, etc.; R4 = H, alkyl; R5 = cycloalkyl, alkanoyl, etc.; p, m = 0-6; r = 2-3); R3 = halo; n = 0-2; R1 = H, alkyl, alkenyl, etc.; R2 = H, alkyl, Ph, Q] were prepared and had antihistaminic and central nervous system depressant activities when tested with guinea pig ileum and in mice, resp. Thus, refluxing 4-methyl-7-(2,3-epoxypropoxy)carbostyril with 4-phenylpiperazine in EtOH 3 h and treating with HCl/EtOH gave 63% 4-methyl-7-[2-hydroxy-(4-phenylpiperazinyl)propoxy]carbostyril-HCl.
IT 76808-65-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 76808-65-6 CAPLUS
CN 2(1H)-Quinolinone, 7-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]propoxy]-3,4-dihydro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L9 ANSWER 82 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:425121 CAPLUS
DOCUMENT NUMBER: 95:25121
TITLE: Antihistaminic carbostyril derivatives
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 44 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

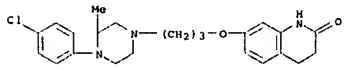
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 55124766 | A | 19800926 | JP 1979-32486 | 19790320 <-- |
| JP 63031445 | B | 19880623 | | |
| PRIORITY APPLN. INFO.: | | | JP 1979-32486 | A 19790320 |

OTHER SOURCE(S): CASREACT 95:25121
GI For diagram(s), see printed CA Issue.
AB Carbostyrils I [R = H, Q (R3 = H, OH, alkyl, etc.; R4 = H, alkyl; R5 = cycloalkyl, alkanoyl, etc.; l,m = 0-6; r = 2, 3); X = halo; n = 0-2; R1 = H, alkyl, etc.; R2 = H, alkyl, Ph, Q] (131 compds.) were prepared and were tested as antihistaminics in guinea pig ileum. Thus, reaction of 4.4 g 5-(2,3-epoxypropoxy)-3,4-dihydrocarbostyril with 3.4 g 1-phenylpiperazine in MeOH 3 h at 50-60° gave, after treating with HCl, 6.5 g 5-[2-hydroxy-3-(4-phenylpiperazinyl)propoxy]-3,4-dihydrocarbostyril-HCl.
IT 76808-65-6P





RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antihistaminic activity of)
RN 76808-65-6 CAPLUS
CN 2(1H)-Quinolinone, 7-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]propoxy]-3,4-dihydro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L9 ANSWER 83 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:192375 CAPLUS
DOCUMENT NUMBER: 94:192375
TITLE: 4-Aryl-5-piperazinoalkyl-1,3-dioxol-2-ones, and compositions
INVENTOR(S): Cascio, Giuseppe; Fregnan, Giancarlo; Manghisi, Elso; Porta, Roberto
PATENT ASSIGNEE(S): Istituto Luso Farmaco d'Italia SpA, Italy
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

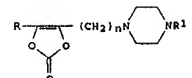
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| US 4235904 | A | 19801125 | US 1979-16135 | 19790301 | <-- |
| AU 7944404 | A | 19790906 | AU 1979-44404 | 19790220 | <-- |
| AU 518565 | B2 | 19811008 | | | |
| CH 639970 | A5 | 19831215 | CH 1979-1825 | 19790223 | <-- |
| FR 2418796 | A1 | 19790928 | FR 1979-4928 | 19790227 | <-- |
| FR 2418796 | B1 | 19810724 | | | |
| ZA 7900922 | A | 19800227 | ZA 1979-922 | 19790227 | <-- |
| CA 1158242 | A1 | 19831206 | CA 1979-322408 | 19790227 | <-- |
| NL 7901583 | A | 19790905 | NL 1979-1583 | 19790228 | <-- |
| NL 177404 | B | 19850416 | | | |
| NL 177404 | C | 19850916 | | | |
| DE 2908148 | A1 | 19790906 | DE 1979-2908148 | 19790302 | <-- |
| DE 2908148 | C2 | 19860807 | | | |
| ES 478696 | A1 | 19800816 | ES 1979-478696 | 19790302 | <-- |
| JP 54130569 | A | 19791009 | JP 1979-25004 | 19790303 | <-- |
| JP 62005155 | B | 19870203 | | | |
| GB 2017684 | A | 19791010 | GB 1979-7651 | 19790305 | <-- |
| GB 2017684 | B | 19820818 | | | |
| PRIORITY APPLN. INFO.: | | | IT 1978-20841 | A 19780303 | |
| | | | IT 1979-48004 | A 19790214 | |

OTHER SOURCE(S): MARPAT 94:192375

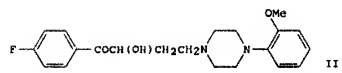




GI

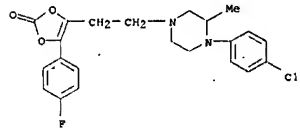


I



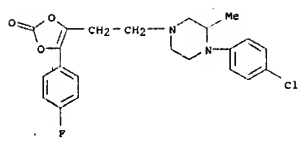
II

AB Piperazinoalkyldioxolones I (R = optionally substituted Ph, naphthyl; R1 = optionally substituted alkyl, Ph, pyridyl, pyrimidinyl; n = 1-3) were prepared Thus II was treated with COCl2 to give I (R = 4-FC6H4, R1 = 2-MeOC6H4, n = 2) which had an antiulcer ED50 of 30 mg/kg orally in rats. I also have anticholesteremic activity.
IT 71923-05-2P 71923-39-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 71923-05-2 CAPLUS
CN 1,3-Dioxol-2-one, 4-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-5-(4-fluorophenyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

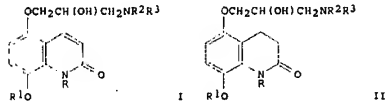
RN 71923-39-2 CAPLUS
CN 1,3-Dioxol-2-one, 4-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-5-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



L9 ANSWER 84 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1980:586412 CAPLUS
DOCUMENT NUMBER: 93:186412
TITLE: Carbostyril compounds
INVENTOR(S): Nakagawa, Kazuyuki; Tominaga, Michiaki; Tone, Hitoshi
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: U.S., 15 pp. Cont.-in-part of U.S. Ser. No. 778,537, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 4210753 | A | 19800701 | US 1978-965470 | 19781130 <-- |
| JP 52113979 | A | 19770924 | JP 1976-28957 | 19760317 <-- |
| JP 59019541 | B | 19840507 | | |
| JP 52136177 | A | 19771114 | JP 1976-52498 | 19760507 <-- |
| JP 60009501 | B | 19850311 | | |
| ZA 7701461 | A | 19780830 | ZA 1977-1461 | 19770310 <-- |
| BE 852556 | A1 | 19770718 | BE 1977-175856 | 19770317 <-- |
| PRIORITY APPLN. INFO.: | | | JP 1976-28957 | A 19760317 |
| | | | JP 1976-52498 | A 19760507 |
| | | | US 1977-778537 | A2 19770317 |

GI



AB 8-Glycidyloxycarbostyrils reacted with amines to give 8-(3-amino-2-hydroxypropoxy)carbostyrils I and II (R = H; R1 = H, phenylalkyl, diphenylalkyl, alkoxyalkyl, hydroxyalkyl, alkanoyl, alkynyl; R2 = H and R3 = pyrrolidinoalkyl, piperazinoalkyl, morpholinoalkyl; or NR2R3 form a piperidino, morpholine, pyrrolidino, or piperazino group), which showed β-adrenergic blocking activity. A mixture of 8-propargyloxy-5-



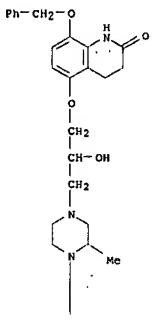


glycidyloxy-3,4-dihydrocarbostyril, pyrrolidine, and MeOH was kept 12 h at 10-15° to give II (R = H, R1 = propargyl, NR2R3 = pyrrolidino).

IT 65008-48-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and β-adrenergic blocking activity of).

RN 65008-48-2 CAPLUS
CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-3,4-dihydro-8-(phenylmethoxy)-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

● HCl

IT 65008-50-6P 65034-66-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

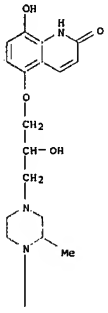
RN 65008-50-6 CAPLUS





CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-8-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

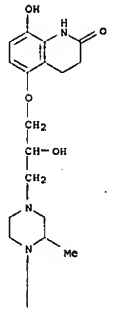
● HCl

RN 65034-66-4 CAPLUS
CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-3,4-dihydro-8-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)





PAGE 1-A

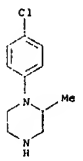


PAGE 2-A

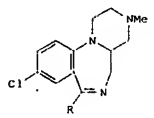
● HCl

IT 55117-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(ring cleavage of (glycidyloxy)carbostyrils by)

RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 85 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1980:542844 CAPLUS
DOCUMENT NUMBER: 93:142844
TITLE: Synthesis and anxiolytic activity of a series of pyrazino[1,2-a][1,4]benzodiazepine derivatives
AUTHOR(S): Smith, R. G.; Lucas, R. A.; Wasley, J. W. F.
CORPORATE SOURCE: Pharm. Div., Ciba-Geigy Corp., Summit, NJ, 07801, USA
SOURCE: Journal of Medicinal Chemistry (1980), 23(8), 952-5
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 93:142844
GI



I

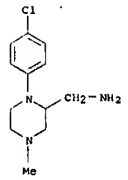
AB The synthesis and biol. evaluation of 5 title compds. I (R = Me, Ph, CH2Ph, and 2- or 4-ClC6H4-) and 2 dihydro derivs. for anxiolytic and antidepressant activities are described. I; R = C6H4Cl-2 [74162-29-1] had significant levels of anxiolytic activity but low antidepressant activity.

IT 74162-26-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation of)

RN 74162-26-8 CAPLUS
CN 2-Piperazinemethanamine, 1-(4-chlorophenyl)-4-methyl- (9CI) (CA INDEX NAME)

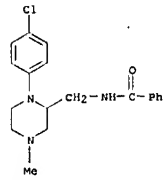




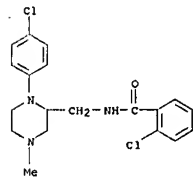


IT 74162-20-2P 74162-21-3P 74162-22-4P
74162-23-5P 74162-24-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of)

RN 74162-20-2 CAPLUS
CN Benzamide, N-[[1-(4-chlorophenyl)-4-methyl-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



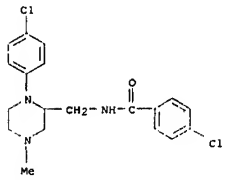
RN 74162-21-3 CAPLUS
CN Benzamide, 2-chloro-N-[[1-(4-chlorophenyl)-4-methyl-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



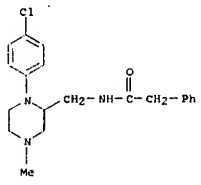




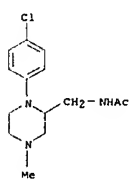
RN 74162-22-4 CAPLUS
CN Benzamide, 4-chloro-N-[[1-(4-chlorophenyl)-4-methyl-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



RN 74162-23-5 CAPLUS
CN Benzeneacetamide, N-[[1-(4-chlorophenyl)-4-methyl-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



RN 74162-24-6 CAPLUS
CN Acetamide, N-[[1-(4-chlorophenyl)-4-methyl-2-piperazinyl]methyl]- (9CI) (CA INDEX NAME)







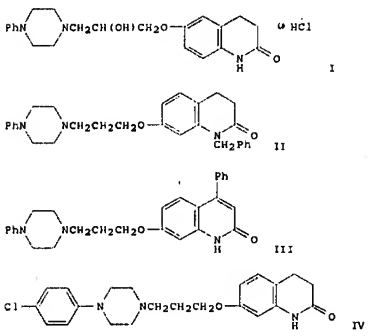
L9 ANSWER 86 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1980:76316 CAPLUS
DOCUMENT NUMBER: 92:76316
TITLE: Carbostyril derivatives
INVENTOR(S): Banno, Kazuo; Fujioka, Takafumi; Oshiro, Yasuo; Nakagawa, Kazuyuki
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Ger. Offen., 166 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 2912105 | A1 | 19791011 | DE 1979-2912105 | 19790327 <--- |
| DE 2912105 | C2 | 19850829 | | |
| DE 2912105 | C3 | 19900215 | | |
| JP 54130587 | A | 19791009 | JP 1978-37783 | 19780330 <--- |
| JP 62023750 | B | 19870525 | | |
| CA 1117110 | A1 | 19820126 | CA 1979-324227 | 19790327 <--- |
| DE 2953723 | C2 | 19860710 | DE 1979-2953723 | 19790327 <--- |
| DE 2953723 | C3 | 19890112 | | |
| FI 7901034 | A | 19791001 | FI 1979-1034 | 19790328 <--- |
| FI 70704 | B | 19860626 | | |
| FI 70704 | C | 19861006 | | |
| AU 7945480 | A | 19791004 | AU 1979-45480 | 19790328 <--- |
| AU 515531 | B2 | 19810409 | | |
| US 4734416 | A | 19880329 | US 1979-24602 | 19790328 <--- |
| BE 875174 | A1 | 19791001 | BE 1979-194281 | 19790329 <--- |
| SE 7902794 | A | 19791001 | SE 1979-2794 | 19790329 <--- |
| SE 434945 | B | 19840827 | | |
| SE 434945 | C | 19841220 | | |
| NO 7901049 | A | 19791002 | NO 1979-1049 | 19790329 <--- |
| NO 151321 | B | 19841210 | | |
| NO 151321 | C | 19850320 | | |
| DK 7901286 | A | 19791026 | DK 1979-1286 | 19790329 <--- |
| DK 158225 | B | 19900416 | | |
| DK 158225 | C | 19900917 | | |
| FR 2421174 | A1 | 19791026 | FR 1979-7863 | 19790329 <--- |
| FR 2421174 | B1 | 19821119 | | |
| CH 641455 | A5 | 19840229 | CH 1979-2953 | 19790329 <--- |
| AT 7902351 | A | 19840415 | AT 1979-2351 | 19790329 <--- |
| AT 376432 | B | 19841126 | | |
| SU 1140687 | A3 | 19850215 | SU 1979-2745704 | 19790329 <--- |
| NL 7902514 | A | 19791002 | NL 1979-2514 | 19790330 <--- |
| NL 183189 | B | 19880316 | | |
| NL 183189 | C | 19880816 | | |
| GB 2017701 | A | 19791010 | GB 1979-11155 | 19790330 <--- |
| GB 2017701 | B | 19830316 | | |
| ZA 7901516 | A | 19800430 | ZA 1979-1516 | 19790330 <--- |
| ES 479134 | A1 | 19800616 | ES 1979-479134 | 19790330 <--- |
| ES 486990 | A1 | 19801001 | ES 1979-486990 | 19791217 <--- |
| ES 486991 | A1 | 19801001 | ES 1979-486991 | 19791217 <--- |
| ES 486992 | A1 | 19801001 | ES 1979-486992 | 19791217 <--- |
| SU 1232144 | A3 | 19860515 | SU 1981-3326599 | 19810908 <--- |
| CH 641350 | A5 | 19840229 | CH 1982-1900 | 19820326 <--- |

| | | | | | |
|---|---|---|---|---|---|
| AT 8303915 | A | 19840415 | AT 1983-3915 | | 19831107 <-- |
| AT 376433 | B | 19841126 | | | |
| AT 8303916 | A | 19840415 | AT 1983-3916 | | 19831107 <-- |
| AT 376434 | B | 19841126 | | | |
| AT 8303917 | A | 19840415 | AT 1983-3917 | | 19831107 <-- |
| AT 376435 | B | 19841126 | | | |
| JP 62149664 | A | 19870703 | JP 1986-295668 | | 19861210 <-- |
| JP 63005387 | B | 19880203 | | | |
| US 4824840 | A | 19890425 | US 1987-25193 | | 19870312 <-- |
| PRIORITY APPLN. INFO.: | | | JP 1978-37783 | A | 19780330 |
| | | | US 1979-24602 | A3 | 19790328 |
| | | | AT 1979-2351 | A | 19790329 |
| | | | CH 1979-2953 | A | 19790329 |

OTHER SOURCE(S): CASREACT 92:76316

GI



AB Apparatus 160 piperazinoalkoxy- (especially-propoxy)-carbostyrils and/or their 3,4-dihydro derivs. were prepared and tested as antihistaminics, anesthesic- and sedative-enhancers, and analgesics; reference compds. were, e.g., haloperidol, diazepam, or pentabarbitol. Any or all of the piperazine, alkoxy, or carbostyril moieties could be substituted. Thus, the compds. were prepared by treatment of the appropriate hydroxycarbostyril with, a dihalo compound (e.g., Br(CH2)3Cl) or an epoxide, then cyclized via conversion into a bis(haloethyl)amine or treated with a piperazine. Compds. prepared included I-IV.

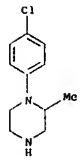
IT 55117-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with carbostyril derivs.)

RN 55117-80-1 CAPLUS

CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)







L9 ANSWER 87 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 1979:593289 CAPLUS |
| DOCUMENT NUMBER: | 91:193289 |
| TITLE: | 4-Aryl-5-aminoalkyl-1,3-dioxol-2-ones and derivatives |
| PATENT ASSIGNEE(S): | Istituto Luso Farmaco d'Italia S.r.l., Italy |
| SOURCE: | Belg., 17 pp.<br>CODEN: BEXXAL |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | Dutch |
| FAMILY ACC. NUM. COUNT: | 2 |
| PATENT INFORMATION: | |

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| BE 874561 | A2 | 19790702 | BE 1979-57638 | 19790302 <-- |
| AU 7944404 | A | 19790906 | AU 1979-44404 | 19790220 <-- |
| AU 518565 | B2 | 19811008 | | |
| CH 639970 | A5 | 19831215 | CH 1979-1825 | 19790223 <-- |
| FR 2418796 | A1 | 19790928 | FR 1979-4928 | 19790227 <-- |
| FR 2418796 | B1 | 19810724 | | |
| ZA 7900922 | A | 19800227 | ZA 1979-922 | 19790227 <-- |
| CA 1158242 | A1 | 19831206 | CA 1979-322408 | 19790227 <-- |
| NL 7901583 | A | 19790905 | NL 1979-1583 | 19790228 <-- |
| NL 177404 | B | 19850416 | | |
| NL 177404 | C | 19850916 | | |
| DE 2908148 | A1 | 19790906 | DE 1979-2908148 | 19790302 <-- |
| DE 2908148 | C2 | 19860807 | | |
| ES 478696 | A1 | 19800816 | ES 1979-478696 | 19790302 <-- |
| JP 54130569 | A | 19791009 | JP 1979-25004 | 19790303 <-- |
| JP 62005155 | B | 19870203 | | |
| GB 2017684 | A | 19791010 | GB 1979-7651 | 19790305 <-- |
| GB 2017684 | B | 19820818 | | |

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | IT 1978-20841 | A | 19780303 |
| | IT 1979-48004 | A | 19790214 |

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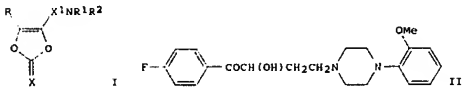
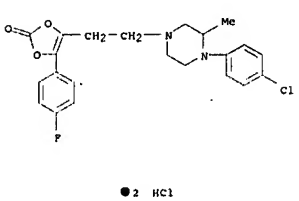


AB Dioxolones I (R = optionally substituted aryl; NR1R2 = secondary amino; X= O, S; X1 = C1-3 alkylene) were prepared Thus, II was treated with COCl2 to give I [R = 4-FC6H4, NR1R2 = 4-(2-methoxyphenyl)piperazino, X = O, X1 = CH2CH2] which had an antiulcer ED30 of 30 mg/kg orally in rats. I also had anticholesteremic activity.

IT 71923-05-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and anticholesteremic and anti-ulcer activity of)

RN 71923-05-2 CAPLUS

CN 1,3-Dioxol-2-one, 4-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-5-(4-fluorophenyl)-, dihydrochloride (9CI) (CA INDEX NAME)

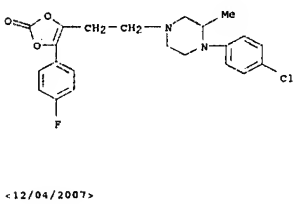


●2 HCl

IT 71923-39-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 71923-39-2 CAPLUS

CN 1,3-Dioxol-2-one, 4-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-5-(4-fluorophenyl)- (9CI) (CA INDEX NAME)







L9 ANSWER 88 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 1979:137696 CAPLUS |
| DOCUMENT NUMBER: | 90:137696 |
| TITLE: | Carbostyrils |
| INVENTOR(S): | Tominaga, Michiaki; Tone, Hitoshi; Nakagawa, Kazuyuki |
| PATENT ASSIGNEE(S): | Otsuka Pharmaceutical Co., Ltd., Japan |
| SOURCE: | Jpn. Kokai Tokkyo Koho, 6 pp.<br>CODEN: JKXXAF |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | Japanese |
| FAMILY ACC. NUM. COUNT: | 1 |
| PATENT INFORMATION: | |

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 53108989 | A | 19780922 | JP 1977-24042 | 19770304 <-- |
| JP 59048830 | B | 19841129 | | |

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|---|---|---|---|
| PRIORITY APPLN. INFO.: | JP 1977-24042 | A | 19770304 |

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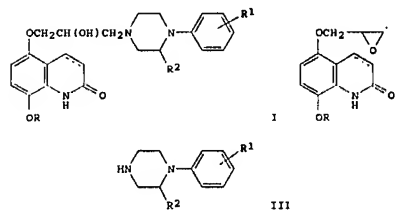


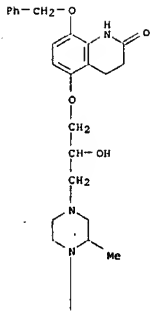
AB Ten carbostyrils I.HCl (R = H, PhCH2; R1 = H, p-MeO or Cl, m-Cl; R2 = H, Me), having β-adrenaline inhibiting activity (no data), were prepared by reaction of II with III. I.HCl (R = H) were also prepared by catalytic reduction of I.HCl (R = PhCH2) over 10% Pd-C. Thus, 2.0 g II (R = PhCH2, 3,4-dihydro) and 2.0 g III (R1 = p-MeO, R2 = H) were stirred in MeOH for 4 h at 40-50° to give 1.2 g I.HCl (R = PhCH2, R1 = p-MeO, R2 = H, 3,4-dihydro).

IT 65008-48-2P 65008-50-6P 65034-66-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 65008-48-2 CAPLUS

CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-3,4-dihydro-8-(phenylmethoxy)-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

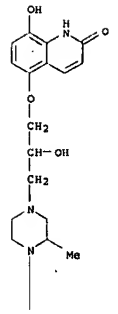
● HCl

RN 65008-50-6 CAPLUS
CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-8-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)





PAGE 1-A



PAGE 2-A

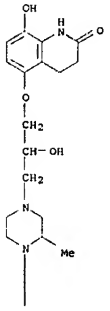
● HCl

RN 65034-66-4 CAPLUS
CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-3,4-dihydro-8-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)





PAGE 1-A



PAGE 2-A

● HCl

L9 ANSWER 89 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1978:37465 CAPLUS
DOCUMENT NUMBER: 88:37465
TITLE: 3-Aminoacrylophenones and some related compounds: a new class of anti-inflammatory agents
AUTHOR(S): Gupta, R. C.; Pratap, Ram; Chatterjee, S. K.; Srimal, R. C.; Anand, Nitya
CORPORATE SOURCE: Cent. Drug Res. Inst., Lucknow, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1977), 15B(7), 641-4
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English





OTHER SOURCE(S): CASREACT 88:37465
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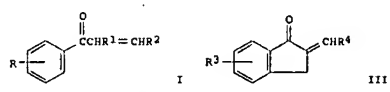
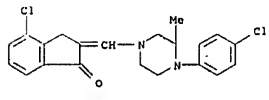


I III

AB Sixteen 3-aminoacrylophenones I (R = 4-F, 2,4-Me2; R1 = H, Me, Et; R2 = piperidino, 4-phenyl-1-piperazinyl, 1-pyrrolidinyl, etc.) (II) were prepared by amination of I (R2 = OH). Similarly 18 2-aminomethylene-1-indanones III (R3 = 4-Cl, 4-, 5-, 6-F; R4 = 4-phenyl-1-piperazinyl, piperidino, etc.) were prepared. Most of II and III have antiinflammatory activity.

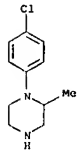
IT 65201-34-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 65201-34-5 CAPLUS
CN 1H-Inden-1-one, 4-chloro-2-[[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]methylene]-2,3-dihydro- (9CI) (CA INDEX NAME)



IT 55117-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with propiophenone)

RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 90 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1978:22663 CAPLUS
DOCUMENT NUMBER: 88:22663

TITLE: Carbostyril derivatives
INVENTOR(S): Tominaga, Michiaki; Tone, Hitochi; Nakagawa, Kazuyuki
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Ger. Offen., 92 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| DE 2711719 | A1 | 19770922 | DE 1977-2711719 | 19770317 | <-- |
| DE 2711719 | C2 | 19850214 | | | |
| JP 52113979 | A | 19770924 | JP 1976-28957 | 19760317 | <-- |
| JP 59019541 | B | 19840507 | | | |
| JP 52136177 | A | 19771114 | JP 1976-52498 | 19760507 | <-- |
| JP 60009501 | B | 19850311 | | | |
| ZA 7701461 | A | 19780830 | ZA 1977-1461 | 19770310 | <-- |
| CH 619453 | A5 | 19800930 | CH 1977-3087 | 19770311 | <-- |
| FI 7700827 | A | 19770918 | FI 1977-827 | 19770315 | <-- |
| FI 63224 | B | 19830131 | | | |
| FI 63224 | C | 19830510 | | | |
| DK 7701156 | A | 19770918 | DK 1977-1156 | 19770316 | <-- |
| DK 154970 | B | 19890116 | | | |
| DK 154970 | C | 19890612 | | | |
| SE 7703000 | A | 19770918 | SE 1977-3000 | 19770316 | <-- |
| SE 443140 | B | 19860217 | | | |
| SE 443140 | C | 19860529 | | | |
| NO 7700940 | A | 19770920 | NO 1977-940 | 19770316 | <-- |
| NO 149388 | B | 19840102 | | | |
| NO 149388 | C | 19840411 | | | |
| AU 7723299 | A | 19780928 | AU 1977-23299 | 19770316 | <-- |
| AU 513950 | B2 | 19810115 | | | |
| BE 852556 | A1 | 19770718 | BE 1977-175856 | 19770317 | <-- |
| NL 7702896 | A | 19770920 | NL 1977-2896 | 19770317 | <-- |
| NL 179816 | B | 19860616 | | | |
| NL 179816 | C | 19861117 | | | |
| FR 2344538 | A1 | 19771014 | FR 1977-8041 | 19770317 | <-- |
| FR 2344538 | B1 | 19800718 | | | |
| CA 1081232 | A1 | 19800708 | CA 1977-274453 | 19770317 | <-- |
| AT 7701815 | A | 19810115 | AT 1977-1815 | 19770317 | <-- |
| AT 363474 | B | 19810810 | | | |

PRIORITY APPLN. INFO.: JP 1976-28957 A 19760317
JP 1976-52498 A 19760507

OTHER SOURCE(S): MARPAT 88:22663
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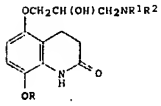


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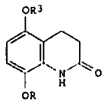



II



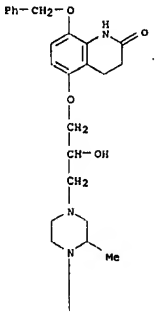


AB Carbostyril derivs. (.apprx.130 compds.), including I (R = H, CH2CH2OMe, allyl, propargyl, CH2Ac, Bu, CH2CH2OH, CH2CO2H, CH2CONH2, Me, CH2Ph, CH2C6H4Ac-4, cyclohexylcarbonyl, CH2CO2Et; R1 = H, R2 = CH2CH2C6H3(OMe)2-3,4, allyl, CMe3, CHPh2, morpholinopropyl, CMe2CH2Ph, CH2CHPh2, CHMe2; NR1R2 = 3-methyl-4-phenylpiperazino) were prepared Thus, II (R = R3 = H) was treated with HC.tplbond.CCH2Br, II (R = CH2C.tplbond.CH, R3 = H) treated with epichlorohydrin, II (R = CH2C.tplbond.CH, R3 = 2,3-epoxypropyl) treated with Me3CNH2 to give I (R = CH2C.tplbond.CH, R1 = H, R2 = CMe3), which at 300 mg/kg i.v. gave 100% inhibition of isoprenalin-induced increase in heart rate in dogs.

IT 65008-48-2P 65008-50-6P 65034-66-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 65008-48-2 CAPLUS
CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-3,4-dihydro-8-(phenylmethoxy)-, monohydrochloride (9CI) (CA INDEX NAME)

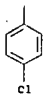
PAGE 1-A







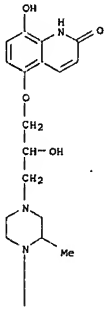

PAGE 2-A




● HCl

RN 65008-50-6 CAPLUS
CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-8-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

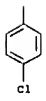
PAGE 1-A







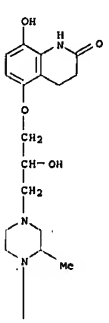

PAGE 2-A




● HCl

RN 65034-66-4 CAPLUS
CN 2(1H)-Quinolinone, 5-[3-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]-2-hydroxypropoxy]-3,4-dihydro-8-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

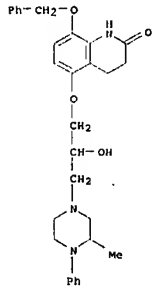
PAGE 1-A



PAGE 2-A

● HCl

IT 65023-17-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sympatholytic activity of)
RN 65023-17-8 CAPLUS
CN 2(1H)-Quinolinone, 3,4-dihydro-5-[2-hydroxy-3-(3-methyl-4-phenyl-1-piperazinyl)propoxy]-8-(phenylmethoxy)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L9 ANSWER 91 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1976:592771 CAPLUS
DOCUMENT NUMBER: 85:192771
TITLE: 8-Aminotheophylline derivatives
INVENTOR(S): Quelet, Jean R.
PATENT ASSIGNEE(S): Laboratoire le Brun S. A., Fr.
SOURCE: Ger. Offen., 15 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German





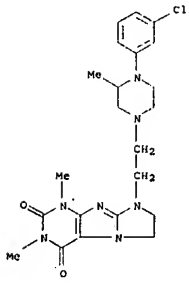
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| DE 2609397 | A1 | 19760923 | DE 1976-2609397 | 19760306 | <-- |
| FR 2303551 | A1 | 19761008 | FR 1975-7675 | 19750312 | <-- |
| ZA 7601234 | A | 19770223 | ZA 1976-1234 | 19760302 | <-- |
| GB 1536492 | A | 19781220 | GB 1976-8487 | 19760303 | <-- |
| JP 51113898 | A | 19761007 | JP 1976-24723 | 19760309 | <-- |
| ES 445944 | A1 | 19770516 | ES 1976-445944 | 19760310 | <-- |
| BE 839419 | A1 | 19760913 | BE 1976-165037 | 19760311 | <-- |
| CH 597231 | A5 | 19780331 | CH 1976-3060 | 19760311 | <-- |
| AU 7611975 | A | 19770915 | AU 1976-11975 | 19760312 | <-- |
| AU 501358 | B2 | 19790621 | | | |

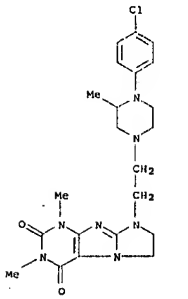
PRIORITY APPLN. INFO.: FR 1975-7675 A 19750312
OTHER SOURCE(S): MARPAT 85:192771
GI For diagram(s), see printed CA Issue.
AB Purinediones [I; R = H, Me, Et, 3-MeOC6H4; R1n = e.g., H, 3-Cl, 3-Br, 3-F, 3,4-Cl2, 3,4-Me2; n = 2, 3, 4; m = 2, 3, 6; (CH2)m = CH2CHMe], with antitussive, antihistaminic, analgesic, inflammation-inhibiting, tranquilizing, and sedative activities, are prepared by reaction of 9-(chloroalkyl)tetrahydropyrimidopurinediones with phenylpiperazines. The pyrimidopurinediones are obtained by condensation of 8-chloro-7-(chloroalkyl)theophyllines with amino alcs. and replacement of the OH with Cl. Thus, reaction of 5.75 g 9-(2-chloroethyl)-6,7,8,9-tetrahydro-1,3-dimethylpyrimido[2,1-f]purine-2,4(1H,3H)-dione with 7.5 g 1-(3-chlorophenyl)piperazine 2 hr at 180-90° gives 4.7 g I (R = H, R1 = 3-Cl, m = 2, n = 3).
IT 60987-61-3P 60987-62-4P 60987-63-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and pharmacol. activity of)
RN 60987-61-3 CAPLUS
CN 1H-Imidazo[2,1-f]purine-2,4(3H,6H)-dione, 8-[2-[4-(3-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-7,8-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)







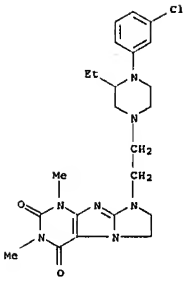
RN 60987-62-4 CAPLUS
CN 1H-Imidazo[2,1-f]purine-2,4(3H,6H)-dione, 8-[2-[4-(4-chlorophenyl)-3-methyl-1-piperazinyl]ethyl]-7,8-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 60987-63-5 CAPLUS
CN 1H-Imidazo[2,1-f]purine-2,4(3H,6H)-dione, 8-[2-[4-(3-chlorophenyl)-3-ethyl-1-piperazinyl]ethyl]-7,8-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



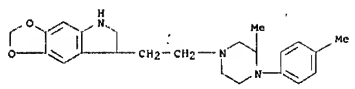




L9 ANSWER 92 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1976:17426 CAPLUS
DOCUMENT NUMBER: 84:17426
TITLE: Aminoalkylenecindolines
INVENTOR(S): Allen, George R., Jr.; Littell, Ruddy
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: Can., 14 pp.
CODEN: CAXXA4
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

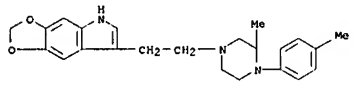
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| CA 972372 | A1 | 19750805 | CA 1972-142893 | 19720524 | <-- |

PRIORITY APPLN. INFO.: US 1972-242734 A 19720410
GI For diagram(s), see printed CA Issue.
AB The title compds. I (R = R1 = MeO; RR1 = OCH2O; R = MeO, R1 = H; R2 = H, Me; R3 = H, Me; R4 = H, 2-MeO, 4-Me, 2-Cl), which reduced motor activity in mice 50% at 0.2-25 mg/ml, were prepared by reduction of the corresponding indoles by hydrogenation in HCl or by Sn-HCl.
IT 49632-90-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 49632-90-8 CAPLUS
CN 5H-1,3-Dioxolo[4,5-f]indole, 6,7-dihydro-7-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]-, trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

IT 40119-10-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reduction of)
RN 40119-10-6 CAPLUS
CN 5H-1,3-Dioxolo[4,5-f]indole, 7-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 93 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1975:443207 CAPLUS
DOCUMENT NUMBER: 83:43207
TITLE: 2-(Piperazinylalkyl)isoquinolinediones
INVENTOR(S): Kutter, Eberhard; Austel, Volkhard; Eberlien, Wolfgang; Heider, Joachim
PATENT ASSIGNEE(S): thomae, Fed. Rep. Ger.
SOURCE: Ger. Offen., 23 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| DE 2345422 | A1 | 19750320 | DE 1973-2345422 | 19730908 | <-- |
| DE 2345422 | C2 | 19831222 | | | |
| AT 7406514 | A | 19751015 | AT 1974-6514 | 19740808 | <-- |
| AT 330777 | B | 19760726 | | | |
| FI 7402465 | A | 19750309 | FI 1974-2465 | 19740821 | <-- |
| FI 52219 | B | 19770331 | | | |
| ES 429473 | A1 | 19760901 | ES 1974-429473 | 19740823 | <-- |
| US 3948898 | A | 19760406 | US 1974-503072 | 19740904 | <-- |
| SU 528035 | A3 | 19760905 | SU 1974-2057995 | 19740904 | <-- |
| AU 7473023 | A | 19760311 | AU 1974-73023 | 19740905 | <-- |
| BE 819651 | A1 | 19750306 | BE 1974-148302 | 19740906 | <-- |
| SE 7411312 | A | 19750310 | SE 1974-11312 | 19740906 | <-- |
| SE 424863 | B | 19820816 | | | |





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| SE 424863 | C | 19821125 | | | |
| NL 7411843 | A | 19750311 | NL 1974-11843 | 19740906 | <-- |
| NL 176363 | B | 19841101 | | | |
| NL 176363 | C | 19850401 | | | |
| NO 7403220 | A | 19750311 | NO 1974-3220 | 19740906 | <-- |
| NO 140978 | B | 19790910 | | | |
| FR 2242979 | A1 | 19750404 | FR 1974-30387 | 19740906 | <-- |
| DK 7404727 | A | 19750505 | DK 1974-4727 | 19740906 | <-- |
| JP 50050381 | A | 19750506 | JP 1974-102862 | 19740906 | <-- |
| JP 59006868 | B | 19840215 | | | |
| DD 115122 | A5 | 19750912 | DD 1974-180966 | 19740906 | <-- |
| HU 167869 | B | 19751225 | HU 1974-TO980 | 19740906 | <-- |
| ZA 7405688 | A | 19760526 | ZA 1974-5688 | 19740906 | <-- |
| GB 1446791 | A | 19760818 | GB 1974-39083 | 19740906 | <-- |
| CH 605778 | A5 | 19781013 | CH 1974-12189 | 19740906 | <-- |
| CH 605779 | A5 | 19781013 | CH 1977-16014 | 19740906 | <-- |
| RO 63655 | A1 | 19781015 | RO 1974-79932 | 19740906 | <-- |
| CS 185660 | B2 | 19781031 | CS 1974-6150 | 19740906 | <-- |
| PL 91712 | B1 | 19770331 | PL 1974-173958 | 19740907 | <-- |
| ES 433958 | A1 | 19761116 | ES 1975-433958 | 19750120 | <-- |
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| AT 334774 | B | 19760110 | | | |
| AT 7505607 | A | 19760515 | AT 1975-5607 | 19750721 | <-- |
| AT 334375 | B | 19760110 | | | |
| US 4021558 | A | 19770503 | US 1976-651568 | 19760122 | <-- |

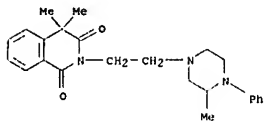
PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| DE 1973-2345422 | A | 19730908 |
| DE 1973-2345423 | A | 19730908 |
| AT 1974-6514 | A | 19740808 |
| US 1974-503072 | A2 | 19740904 |

GI For diagram(s), see printed CA Issue.
AB Twenty-five isoquinolinediones I (R = Ph, substituted Ph, or 2-pyridyl; R1 = H or Me; R2 = H, F, Cl, or MeO; n = 2 or 3), useful as antihypertensives or sedatives or in tachycardia treatment (no data), were prepared by reaction of the isochromandiones (II, X = O) or isoquinolinediones II (X = NH) with (1-piperazinyl)alkylamines or (1-piperazinyl)alkyl chlorides, resp., or by reaction of the isoquinolinediones (II, X = N(CH2)nCl] with the piperazines.
IT 55974-45-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of antihypertensive and sedative)
RN 55974-45-3 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 4,4-dimethyl-2-[2-[3-methyl-4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)







●2 HCl

IT 2946-76-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with isoquinolinediones)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

L9 ANSWER 94 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1975:171026 CAPLUS
DOCUMENT NUMBER: 82:171026
TITLE: 1,3-Dialkyl-4-aminouracils
INVENTOR(S): Hartleben, York; Goering, Joachim; Tauscher, Manfred; Rohte, Oskar; Brenner, Guenter; Firma Johann A. Wuelfing
SOURCE: Ger. Offen., 25 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| DE 2329399 | A1 | 19750102 | DE 1973-2329399 | 19730608 | <-- |
| FI 7401579 | A | 19741209 | FI 1974-1579 | 19740523 | <-- |
| AT 7404300 | A | 19760115 | AT 1974-4300 | 19740524 | <-- |
| AT 332425 | B | 19760927 | | | |
| JP 50052077 | A | 19750509 | JP 1974-62447 | 19740601 | <-- |
| SE 7407471 | A | 19741209 | SE 1974-7471 | 19740606 | <-- |
| NL 7407611 | A | 19741210 | NL 1974-7611 | 19740606 | <-- |
| BE 816055 | A1 | 19740930 | BE 1974-145190 | 19740607 | <-- |
| FR 2232320 | A1 | 19750103 | FR 1974-19693 | 19740607 | <-- |
| HU 168153 | B | 19760228 | HU 1974-WU16 | 19740607 | <-- |
| DD 119233 | A5 | 19760412 | DD 1974-179053 | 19740610 | <-- |

PRIORITY APPLN. INFO.:

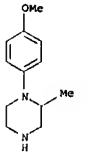
| | | |
|---|---|---|
| DE 1973-2329399 | A | 19730608 |

GI For diagram(s), see printed CA Issue.

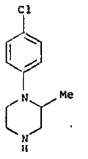




AB About 40 uracils I and II [R = Me, Me2CH, or Bu; R1 = CH2CH2OH, CH2CH2SO2C6H4Me-4, or (CH2)3OH; R2 = Me, Pr, CH2CHMeOH, CH2Ph, (CH2)3NH2, CO2Et, C6H4COMe-4 or -2, 2-pyridyl, CHPhC6H4Cl-4, etc.; R3 = H or Me] were prepared by reaction of 4-chlorouracils with amines. I and II had anticholesteremic, choleretic, and diuretic activity when tested orally in the rat. LD50 values were obtained in the mouse. Thus, 1,3-dibutyl-4-chlorouracil and H2NCH2CH2OH were refluxed in EtOH to give 97% I (R = Bu, R1 = CH2CH2OH).
IT 35947-12-7 55117-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with chlorouracils)
RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)

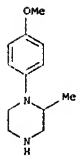


RN 55117-80-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-2-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 95 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1975:170836 CAPLUS
DOCUMENT NUMBER: 82:170836
TITLE: Synthesis of new piperazine derivatives. 1-Alkyl(or aroyl)-4-(N-alkyl(or aroyl) piperazinyl)-1-butene-3-ones
AUTHOR(S): Baboulene, Michel; Sturtz, Georges
CORPORATE SOURCE: Lab. Chim. Hetero-Org., U.E.R. Sci., Brest, Fr.
SOURCE: Comptes Rendus des Seances de l'Academie des Sciences, Serie C: Sciences Chimiques (1975), 280(3), 149-51

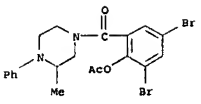
CODEN: CHDCAQ; ISSN: 0567-6541
DOCUMENT TYPE: Journal
LANGUAGE: French
OTHER SOURCE(S): CASREACT 82:170836
GI For diagram(s), see printed CA Issue.
AB Piperazines I(R=Me, Ph, 4-FC6H4, 4-MeOC3H4, Ch2Ph; R1=CHMe2, Ph, 4-BrC6H4, 4-FC6H4, 4-MeC6H4) were prepared in 25-45% yield by treating the phosphonates II with R1CHO. II were prepared in .apprx.95% yield by treating (EtO)2P(O)CH2CBr:CHBr with Et2NH, hydrolyzing (EtO)2P(O)CH:C(NEt2)CH2Br, and treating (EtO)2P(O)CH2COCH2Br with the piperazine derivs. Ketones did not react with II.
IT 35947-12-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with bromo(oxo)alkylphosphonate)
RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 96 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1974:552164 CAPLUS
DOCUMENT NUMBER: 81:152164
TITLE: Possible anti-Parkinsonian compounds. II. Synthesis of 3,5-dihalo acetyl salicyloylamines, piperazines, and phenothiazines
AUTHOR(S): Tiwari, S. S.; Pandey, V. K.
CORPORATE SOURCE: Dep. Chem., Lucknow Univ., Luchnow, India
SOURCE: Journal of the Indian Chemical Society (1973), 50(12), 800-1
CODEN: JICSAH; ISSN: 0019-4522
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Dihaloacetylsalicylamides I (R = Cl, Br; R1 = R2 = Me, Et, Ph, CH2CH2OH; NR1R2 = morpholino, piperidino, pyrrolidino, phenothiazino, N-arylpiperazino) were prepared by acylating the dihalosalicylic acids, chlorinating, and treating with the amine.
IT 54295-55-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 54295-55-5 CAPLUS
CN Piperazine, 4-[2-(acetyloxy)-3,5-dibromobenzoyl]-2-methyl-1-phenyl- (9CI) (CA INDEX NAME)







IT 2946-76-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with acetyldihalosalicoyl chlorides)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

L9 ANSWER 97 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1974:141107 CAPLUS
DOCUMENT NUMBER: 80:141107
TITLE: Pharmacological analysis of the role of the nervous system in inflammation
AUTHOR(S): Trinus, F. P.
CORPORATE SOURCE: Kiev, USSR
SOURCE: Farmakologiya i Toksikologiya (Kiev) (1973), No. 6, 40-7
CODEN: FATOBP; ISSN: 0430-0939
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Seven compds. which affect the central nervous system and 17 compds. which affect the autonomic nervous system were tested for their antiinflammatory effects in rats with formalin induced inflammation. Compds. which inhibit the central nervous system, such as chloral hydrate [302-17-0], hexenal [50-09-9], aminazine [50-53-3], and reserpine [50-55-5], were antiinflammatory, whereas central nervous system stimulators were not. The ganglion stimulator, dimethylphenylpiperazine [33905-48-5], had a short-acting antiinflammatory effect, whereas gangliolytics did not. The cholinomimetic, carbachol [51-83-2], the anticholinesterases, eserine [57-47-6] and proserine [114-80-7], the sympathomimetics, adrenaline [51-43-4], octadine [60-02-6], the α-adrenolytics, dihydroergotoxin [11032-41-0] and phentolamine [50-60-2], and the monoamine oxidase inhibitors ipraxide [54-92-2], malamide [4387-09-1], and transamine [3721-28-6] were also antiinflammatory.

L9 ANSWER 98 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1973:492287 CAPLUS
DOCUMENT NUMBER: 79:92287
TITLE: 1-Acyl-3-(2-[4-phenyl-1-piperazinyl]ethyl]indolines
INVENTOR(S): Allen, George Rodger, Jr.; McEvoy, Francis J.; De Vries, Vern G.; Moran, Daniel B.; Littell, Ruddy
PATENT ASSIGNEE(S): American Cyanamid Co.
SOURCE: U.S., 14 pp.

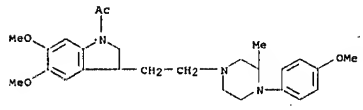




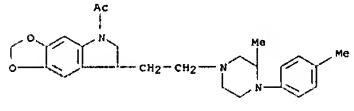
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 3751417 | A | 19730807 | US 1971-171319 | 19710812 <-- |
| PRIORITY APPLN. INFO.: | | | US 1971-171319 A | 19710812 |

GI For diagram(s), see printed CA Issue.
AB Preparation of the title indoline derivs. with analgesic properties is described. In an example, 1-acetyl-3-indolineacetic acid (I) was reduced (borane/THF) to the alc. II which on treatment with PBr3 gave III. III on reaction with 1-phenylpiperazine gave IV (R1 = R2 = R3 = H, R4 = Ac). Also reported are IV [R1 = 5,6-(MeO)2, 5,6-methylenedioxy; R2 = H, Me; R3 = H, MeO; R4 = Bz, p-ClC6H4CO, p-O2NC6H4CO, EtCO, Ac, PrCO].
IT 40118-64-7P 40118-66-9P 49632-90-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 40118-64-7 CAPLUS
CN 1H-Indole, 1-acetyl-2,3-dihydro-5,6-dimethoxy-3-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



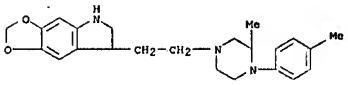
RN 40118-66-9 CAPLUS
CN 5H-1,3-Dioxolo[4,5-f]indole, 5-acetyl-6,7-dihydro-7-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 49632-90-8 CAPLUS
CN 5H-1,3-Dioxolo[4,5-f]indole, 6,7-dihydro-7-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]-, trihydrochloride (9CI) (CA INDEX NAME)

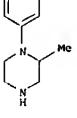




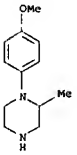


●3 HCl

IT 35947-11-6 35947-12-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (bromoethyl)indolines)
RN 35947-11-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)- (CA INDEX NAME)



RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



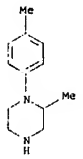
L9 ANSWER 99 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1973:417847 CAPLUS
DOCUMENT NUMBER: 79:17847
TITLE: Thermodynamics of the complexing of silver by piperazine and some of its derivatives in water-ethanol solution

AUTHOR(S): Enea, O.; Houngbossa, K.; Berthon, G.
CORPORATE SOURCE: Lab. Thermodyn. Chim. Electrochim., Univ. Poitiers, Poitiers, Fr.
SOURCE: Thermochimica Acta (1973), 6(3), 309-17
CODEN: THACAS; ISSN: 0040-6031
DOCUMENT TYPE: Journal
LANGUAGE: French

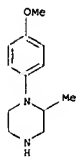
AB The stability consts. of the complexes of $Ag^+$ ion with piperazine and its 2-methyl-, 2-methyl-1-m-tolyl-, 2-methyl-1-p-tolyl-, and 1-(p-methoxyphenyl)-2-methyl- derivs. are obtained at 25° in water-EtOH (52%, w/w) and KNO3 0.1 M ionic strength, by means of corresponding metal-complex electrodes. The enthalpies of formation are determined by direct calorimetry. The thermodn. functions $\Delta G_n°$, $\Delta H_n°$, $\Delta S_n°$ are discussed in relation to the ability of each amine to coordinate, in terms of the nature and position of the entering group.

IT 35947-11-6 35947-12-7
RL: PROC (Process)
(complex formation of, with silver ion, stability of)

RN 35947-11-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)- (CA INDEX NAME)



RN 35947-12-7 CAPLUS
CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 100 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1973:84255 CAPLUS
DOCUMENT NUMBER: 78:84255





TITLE: 3-[2-(4-Phenyl-1-piperazinyl)ethyl]indolines
INVENTOR(S): Allen, George Rodger, Jr.; McEvoy, Francis Joseph; DeVries, Vern Gordon; Moran, Daiel Bryan; Litell, Ruddy
PATENT ASSIGNEE(S): American Cyanamid Co.
SOURCE: Ger. Offen., 87 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| DE 2225765 | A | 19721207 | DE 1972-2225765 | 19720526 | <-- |
| US 3751416 | A | 19730807 | US 1971-147700 | 19710527 | <-- |
| ZA 7202916 | A | 19730228 | ZA 1972-2916 | 19720501 | <-- |
| CA 1014154 | A1 | 19770719 | CA 1972-140989 | 19720501 | <-- |
| GB 1382916 | A | 19750205 | GB 1972-20674 | 19720503 | <-- |
| GB 1382917 | A | 19750205 | GB 1973-56237 | 19720503 | <-- |
| AU 7241918 | A | 19731108 | AU 1972-41918 | 19720504 | <-- |
| CS 185203 | B2 | 19780915 | CS 1972-3454 | 19720519 | <-- |
| CS 185244 | B2 | 19780915 | CS 1976-248 | 19720519 | <-- |
| CS 185245 | B2 | 19780915 | CS 1976-251 | 19720519 | <-- |
| PL 81987 | B1 | 19751031 | PL 1972-155596 | 19720525 | <-- |
| PL 92627 | B1 | 19770430 | PL 1972-176212 | 19720525 | <-- |
| PL 92635 | B1 | 19770430 | PL 1972-176213 | 19720525 | <-- |
| PL 92634 | B1 | 19770430 | PL 1972-176214 | 19720525 | <-- |
| BE 784012 | A1 | 19721127 | BE 1972-117944 | 19720526 | <-- |
| NL 7207129 | A | 19721129 | NL 1972-7129 | 19720526 | <-- |
| FR 2139158 | A1 | 19730105 | FR 1972-18968 | 19720526 | <-- |
| DD 100471 | A5 | 19730920 | DD 1972-163237 | 19720526 | <-- |
| SU 489321 | A3 | 19751025 | SU 1972-1792254 | 19720526 | <-- |
| SU 489322 | A3 | 19751025 | SU 1972-1960739 | 19720526 | <-- |
| CH 579563 | A5 | 19760915 | CH 1972-7843 | 19720526 | <-- |
| RO 60145 | A1 | 19760915 | RO 1972-71032 | 19720526 | <-- |
| CH 582142 | A5 | 19761130 | CH 1976-7597 | 19720526 | <-- |
| CH 582172 | A5 | 19761130 | CH 1976-7598 | 19720526 | <-- |
| CH 583700 | A5 | 19770114 | CH 1976-7595 | 19720526 | <-- |
| CH 583701 | A5 | 19770114 | CH 1976-7596 | 19720526 | <-- |
| NO 136795 | B | 19770801 | NO 1972-1869 | 19720526 | <-- |
| SE 395455 | B | 19770815 | SE 1972-6918 | 19720526 | <-- |
| SE 397524 | B | 19771107 | SE 1974-2374 | 19720526 | <-- |
| SE 397525 | B | 19771107 | SE 1974-2375 | 19720526 | <-- |
| RO 63715 | A1 | 19781015 | RO 1972-80196 | 19720526 | <-- |
| RO 63730 | A1 | 19781115 | RO 1972-80194 | 19720526 | <-- |
| RO 64489 | A1 | 19790515 | RO 1972-80193 | 19720526 | <-- |
| HU 166178 | B | 19750228 | HU 1972-AE360 | 19720527 | <-- |
| HU 167203 | B | 19750927 | HU 1972-AE400 | 19720527 | <-- |
| HU 168720 | B | 19760728 | HU 1972-AE401 | 19720527 | <-- |
| ES 409281 | A1 | 19760316 | ES 1972-409281 | 19721204 | <-- |
| ES 409282 | A1 | 19760316 | ES 1972-409282 | 19721204 | <-- |
| ES 409283 | A1 | 19760316 | ES 1972-409283 | 19721204 | <-- |
| ES 409284 | A1 | 19760316 | ES 1972-409284 | 19721204 | <-- |
| US 3900495 | A | 19750819 | US 1973-350445 | 19730412 | <-- |
| SU 575024 | A3 | 19770930 | SU 1973-1953507 | 19730726 | <-- |
| SU 488408 | A3 | 19751015 | SU 1973-1960738 | 19730913 | <-- |
| SE 7600531 | A | 19760120 | SE 1976-531 | 19760120 | <-- |
| CA 1056821 | A2 | 19790619 | CA 1977-276961 | 19770426 | <-- |





PRIORITY APPLN. INFO.:

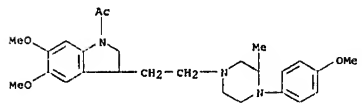
| | | |
|---|---|---|
| US 1971-147700 | A | 19710527 |
| CA 1972-140989 | A3 | 19720501 |
| ES 1972-403245 | A3 | 19720527 |

GI For diagram(s), see printed CA Issue.

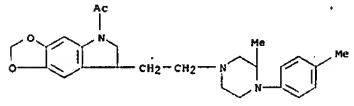
AB Approx. 60 piperazinylethylindolines I (R = Ac, Bz, H, etc.; R1 = Me, H; R2 = H, o-, p-MeO, o-, m-Me, o-, m-Cl, etc.; R3 = H, MeO, Br, O2N, Ac, etc.; R4 = MeO), tranquilizers, were prepared by reaction of a piperazine with a 3-(2-bromoethyl)indoline. Dosages of I for 50% reduction of motor activity in mice were given.

IT 40118-64-7P 40118-66-9P 40118-85-2P
40119-01-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

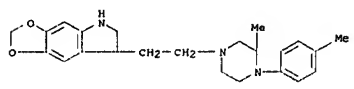
RN 40118-64-7 CAPLUS
CN 1H-Indole, 1-acetyl-2,3-dihydro-5,6-dimethoxy-3-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 40118-66-9 CAPLUS
CN 5H-1,3-Dioxolo[4,5-f]indole, 5-acetyl-6,7-dihydro-7-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



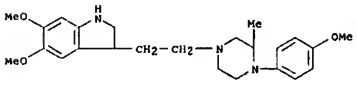
RN 40118-85-2 CAPLUS
CN 5H-1,3-Dioxolo[4,5-f]indole, 6,7-dihydro-7-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 40119-01-5 CAPLUS
CN 1H-Indole, 2,3-dihydro-5,6-dimethoxy-3-[2-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

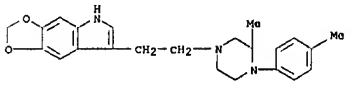






IT 40119-10-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reduction of)

RN 40119-10-6 CAPLUS
CN 5H-1,3-Dioxolo[4,5-f]indole, 7-[2-[3-methyl-4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

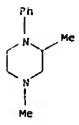


L9 ANSWER 101 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1972:405077 CAPLUS
DOCUMENT NUMBER: 77:5077
TITLE: Syntheses of heterocyclic compounds. CDLX. Benzyne reaction. XIII. Benzyne reaction of halogenobenzenes with N-alkylmorpholines
AUTHOR(S): Kametani, T.; Kigasawa, K.; Hiiragi, M.; Aoyama, T.
CORPORATE SOURCE: Pharm. Inst., Tohoku Univ., Sendai, Japan
SOURCE: Journal of Organic Chemistry (1972), 37(9), 1450-3
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 77:5077

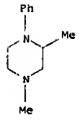
AB The benzyne reaction of N-alkylmorpholines with bromobenzene in the presence of NaNH2 gives mixts. of N-alkylanilines and N-alkyl-N-(β-hydroxyethyl)anilines. Minor amts. of ylide rearrangement products were obtained with other tertiary amines.

IT 33905-48-5P 33905-49-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 33905-48-5 CAPLUS
CN Piperazine, 2,4-dimethyl-1-phenyl- (9CI) (CA INDEX NAME)



RN 33905-49-6 CAPLUS
CN Piperazine, 2,4-dimethyl-1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)



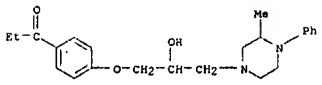
● HCl

L9 ANSWER 102 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1972:149138 CAPLUS
DOCUMENT NUMBER: 76:149138
TITLE: Agents acting on the central nervous system. 14. 1-(p-alkanoylphenoxy)-3-(N4-arylpiperazinyl)propan-2-ols. New class of antidepressants
AUTHOR(S): Rastogi, S. Nivas; Anand, Nitya; Prasad, C. R.
CORPORATE SOURCE: Div. Med. Chem., Cent. Drug Res. Inst., Lucknow, India
SOURCE: Journal of Medicinal Chemistry (1972), 15(3), 286-91
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 76:149138
AB 1-(P-alkanoylphenoxy)-3-(4-piperazinyl)-2-propanols (I), 1,3-bis(aryloxy)-2-propanols (II) and related compds. were prepared, e.g., by condensation of 1-aryloxy-2,3-epoxypropanes with amines and screened pharmacol. 1-(P-propionylphenoxy)-3-(4-phenylpiperazinyl)-2-propanol (III) [34675-77-9] counteracted reserpine-induced depression in cats and potentiated amphetamine-induced stimulation in mice and rats at 5-10 mg/kg; at 100 mg/kg, III counteracted amphetamine-induced hyperactivity and toxicity in aggregated mice. Structural modifications of II gave decreased antidepressant activity, thus III activity is specific and very similar to that of amitriptyline [50-48-6] and imipramine [50-49-7].
IT 36115-92-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacology of)

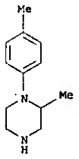




RN 36115-92-1 CAPLUS
CN 1-Propanone, 1-[4-[2-hydroxy-3-(3-methyl-4-phenyl-1-piperazinyl)propoxy]phenyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 103 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1972:90929 CAPLUS
DOCUMENT NUMBER: 76:90929
TITLE: Heats of protonation of piperazine and some derivatives in water-ethanol media
AUTHOR(S): Berthon, Guy; Enea, Octav; Houngbossa, Kouassi
CORPORATE SOURCE: Lab. Thermodyn. Chim. Electrochim., Univ. Poitiers, Poitiers, Fr.
SOURCE: Comptes Rendus des Seances de l'Academie des Sciences, Serie C: Sciences Chimiques (1971), 273(18), 1140-3
CODEN: CHDCAQ; ISSN: 0567-6541
DOCUMENT TYPE: Journal
LANGUAGE: French
AB At 25° with water-52% EtOH as solvent and ionic strength 0.1 mole/dm3 (KNO3), the standard Gibbs free energies (in kcal/mole), standard enthalpies (in kcal/mole), and standard entropies (in cal/degree mole), resp., for the protonation reactions AHn-1(n-1)+ + H+ ↔ AHn+ (n = 1,2) are: piperazine -12.60, -10.5, +7.0 for n = 1, -7.10, -7.0, 0 for n = 2; 2-methylpiperazine -12.22, -10.4, +6.1 for n = 1, -6.98, -6.4, +1.9 for n = 2; 2-methyl-1-m-tolylpiperazine -11.12, -8.8, +7.8 for n = 1; 2-methyl-1-p-tolylpiperazine -11.17, -8.1, +10.0 for n = 1; 1-(p-methoxyphenyl)-2-methylpiperazine -11.23, -8.4, +9.5 for n = 1.
IT 35947-11-6 35947-12-7
RL: PROC (Process)
(thermodynamics of protonation of)
RN 35947-11-6 CAPLUS
CN Piperazine, 2-methyl-1-(4-methylphenyl)- (CA INDEX NAME)

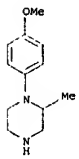


RN 35947-12-7 CAPLUS





CN Piperazine, 1-(4-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 104 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1972:72551 CAPLUS
DOCUMENT NUMBER: 76:72551
TITLE: 5-(2-Aminoethyl)-2,3-piperazinediones and 3-(2-aminoethyl)piperazines
INVENTOR(S): Lunsford, Carl D.; Cale, Albert D., Jr.
PATENT ASSIGNEE(S): A. H. Robins Co., Inc.
SOURCE: Ger. Offen., 28 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

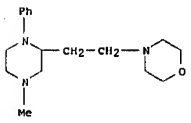
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| DE 2120367 | A | 19711111 | DE 1971-2120367 | 19710426 | <-- |
| ES 389548 | A1 | 19730616 | ES 1971-389548 | 19710325 | <-- |
| GB 1340894 | A | 19731219 | GB 1971-10219 | 19710420 | <-- |
| FR 2092096 | A1 | 19720121 | FR 1971-14802 | 19710426 | <-- |
| FR 2092096 | A5 | 19720121 | | | |
| ZA 7102663 | A | 19720126 | ZA 1971-2663 | 19710426 | <-- |
| CH 534685 | A | 19730430 | CH 1971-6092 | 19710426 | <-- |
| US 3862938 | A | 19750128 | US 1972-230459 | 19720229 | <-- |
| PRIORITY APPLN. INFO.: | | | US 1970-32346 | A 19700427 | |

GI For diagram(s), see printed CA Issue.
AB Title compds., useful as antiviral agents against myxoviruses, were prepared by reaction of 5-(2-chloroethyl)-2,3-piperazinediones with amines to give the corresponding aminoethylpiperazinediones (I) and reduction of I with LiAlH4 to give the piperazines (II). Thus, I (R = Me, R1 = Cl) was refluxed 4 hr in morpholine to give 70 I (R = Me, R1 = morpholino) (III). Similarly prepared were 7 addnl. I, e.g. (R and R1 given): iso-Pr, morpholino (IV); iso-Pr, NMe2 (V); cyclohexyl, morpholino (VI); cyclohexyl, NMe2 (VII). III was refluxed 4 hr with LiAlH4 in THF to give 60% II (R = Me, R1 = morpholino). Similarly prepared were II (R and R1 given): Et, morpholino; cyclohexyl, morpholino (VIII); cyclohexyl, NMe2. IV, VII, and VIII were active against influenza, V, VI, and VII against parainfluenza type III, and VII was active against respiratory syncytial virus.
IT 34933-34-1P 34933-35-2P 34933-38-5P
RL: SPN (Synthetic preparation); PREP (Preparation)

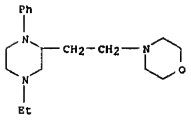




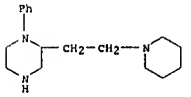
(preparation of)
RN 34933-34-1 CAPLUS
CN Morpholine, 4-[2-(4-methyl-1-phenyl-2-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 34933-35-2 CAPLUS
CN Morpholine, 4-[2-(4-ethyl-1-phenyl-2-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

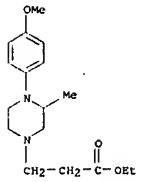


RN 34933-38-5 CAPLUS
CN Piperazine, 1-phenyl-2-[2-(1-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



L9 ANSWER 105 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1971:139148 CAPLUS
DOCUMENT NUMBER: 74:139148
TITLE: Effects of morpholino-, pyrrolidino-, piperazino-, and cyclooctyl-derivatives of β-alanine on brain amines and amino acids
AUTHOR(S): Leonard, Brian E.; Liska, Kenneth J.
CORPORATE SOURCE: Imp. Chem. Ind. Ltd., Cheshire, UK
SOURCE: Life Sciences (1971), 10(2)(Pt. 1), 93-104
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English

GI For diagram(s), see printed CA Issue.
AB Eight β-alanine derivs., related structurally to the D-ring of lysergic acid diethylamide (LSD), were synthesized and examined for psychotomimetic activity in rats. On the basis of 11 parameters studied, such as behavioral effects, hyperthermia, and effects on brain catechol amines, little similarity was observed between these derivs. and LSD. Et 3-(cyclooctylamino)propionate (I) exhibited the action profile most like LSD, followed by 3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]-N,N-diethylpropionamide (II), Et 3-[4-(4-methoxyphenyl)-3-methyl-1-piperazinyl]propionate (III), and 3-[2-(1-pyrrolidinyl)ethylamino]-N,N-diethylpropionamide. 3-(2-Mor-pholinoethylamino)-N,N-diethylpropionamide showed no neurochem. effects similar to LSD.
IT 32559-61-8 32835-69-1
RL: BIOL (Biological study)
(brain amino acids and pyrocatechol amines in response to)
RN 32559-61-8 CAPLUS
CN 1-Piperazinepropanoic acid, 4-(4-methoxyphenyl)-3-methyl-, ethyl ester, hydrochloride (9CI) (CA INDEX NAME)

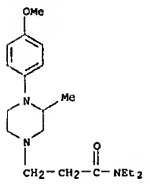


●x HCl

RN 32835-69-1 CAPLUS
CN 1-Piperazinepropanamide, N,N-diethyl-4-(4-methoxyphenyl)-3-methyl-, hydrochloride (9CI) (CA INDEX NAME)







●x HCl

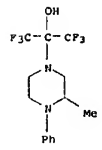
L9 ANSWER 106 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1970:78383 CAPLUS
DOCUMENT NUMBER: 72:78383
TITLE: Herbicidal halogen-containing amino alcohols
PATENT ASSIGNEE(S): Esso Research and Engineering Co.
SOURCE: Brit., 19 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| GB 1178420 | | 19700121 | GB 1967-46007 | 19671009 <-- |
| DE 1643315 | | | DE | |
| US 3520929 | | 19700721 | US | 19661019 <-- |
| PRIORITY APPLN. INFO.: | | | US | 19661019 |

AB Herbicidal and fungicidal title compds. were prepared by reaction of halo ketones and aldehydes with amines. Thus 83 g (F3C)2O was passed into a solution of 60 g N,N-dimethyl-1,3-propanediamine in 200 ml Et2O at -50° to give 2-[3-(dimethylamino)propylamino]-1,1,1,3,3,3-hexafluoro-2-propanol, m. 62.5-3.5°. Similarly 58 compds. were prepared, and screened as pre- and postemergent herbicides at 10 lbs/acre on millet, ryegrass, sorghum, aster, buckwheat, and turnip. Bean rust fungus Uromyces phaseoli and Erysiphe polygoni bean mildew were controlled by 1000 ppm of most of the compds. tested.
IT 26799-46-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 26799-46-2 CAPLUS
CN 1-Piperazinemethanol, 3-methyl-4-phenyl-α,α-bis(trifluoromethyl)- (8CI) (CA INDEX NAME)



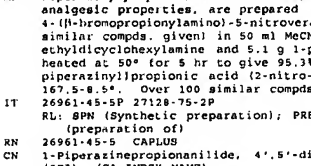




L9 ANSWER 107 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1970:66985 CAPLUS
DOCUMENT NUMBER: 72:66985
TITLE: Piperazinyl derivatives
PATENT ASSIGNEE(S): Byk-Gulden Lomberg Chemische Fabrik G.m.b.H.
SOURCE: Brit., 9 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| GB 1166595 | | 19691008 | GB 1968-8503 | 19680221 <-- |
| DE 1670200 | | | DE | |
| FR 1577338 | | | FR | |
| PRIORITY APPLN. INFO.: | | | DE | 19670322 |

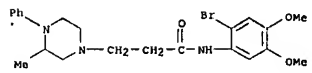
AB Piperazinylpropionic acid anilides, useful for sedative, neuroleptic, and analgesic properties, are prepared Thus, a hot solution of 10 g 4-(β-bromopropionylamino)-5-nitroveratrole (preparation of this and similar compds. given) in 50 ml MeCN is slowly poured into a solution of 6 g ethyldicyclohexylamine and 5.1 g 1-phenylpiperazine in 50 ml EtOH and heated at 50° for 5 hr to give 95.3% β-(1-phenyl-4-piperazinyl)propionic acid (2-nitro-4,5-dimethoxy)anilide, m. 167.5-8.5°. Over 100 similar compds. are described.
IT 26961-45-5P 27128-75-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 26961-45-5 CAPLUS
CN 1-Piperazinepropionanilide, 4',5'-dimethoxy-3-methyl-2'-nitro-4-phenyl- (8CI) (CA INDEX NAME)



RN 27128-75-2 CAPLUS
CN 1-Piperazinepropionanilide, 2'-bromo-4',5'-dimethoxy-3-methyl-4-phenyl- (8CI) (CA INDEX NAME)





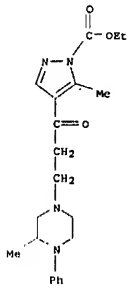


L9. ANSWER 108 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1969:78009 CAPLUS
DOCUMENT NUMBER: 70:78009
TITLE: N-[2-(Pyrazol-4-ylcarbonyl)ethyl]-N-arylpiperazines
PATENT ASSIGNEE(S): CIBA Ltd.
SOURCE: Fr., 23 pp.
CODEN: FRXXAK
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| FR 1510206 | | 19680119 | FR 1966-87512 | 19661215 <-- |
| US 3470184 | | 19690930 | US | 19661222 <-- |
| PRIORITY APPLN. INFO.: | | | CH | 19651223 |
| | | | CH | 19661110 |

GI For diagram(s), see printed CA Issue.
AB Pyrazol-4-ylcarbonylethyl piperazines (I), useful as hypotensive agents, are prepared A mixture of 9.8 g. 4-acetyl-1-carbethoxy-5-methylpyrazole (II), 4.5 g. paraformaldehyde, 12.5 g. N-(2-methylphenyl)-piperazine-2HCl, 8 drops concentrated HCl, and 150 ml. EtOH is refluxed overnight to give N-[3-(1-carbethoxy-5-methyl-4-pyrazolyl)-3-oxo-propyl]-N'-(2-methylphenyl)piperazine, HCl salt m. 214-15° (decomposition). Similarly prepared are the following I (X = OEt, R = Me) (Ar and m.p. HCl salt given): o-ClC6H4, 215-16° (decomposition); p-FC6H4, 215° (decomposition); o-MeOC6H4, 202-3° (decomposition); o-EtC6H4, 190° (decomposition); p-tolyl, -, 2HCl salt m. 195° (decomposition); m-ClC6H4, 205° (decomposition); 2-pyridyl, -, maleate m. 170°; m-F3CC6H4, 190-1° (decomposition); p-ClC6H4,196-7° (decomposition); 4-pyridyl, -, maleate m. 176-7°; o-FC6H4, 290° (decomposition); o-F3CC6H4, 198° (decomposition); and the following compds. (salt m.p. given): I (X = OEt, R = Ph, Ar = p-FC6H4), maleate dihydrate 15 3-4°; I (X = Ph, R = Me, Ar = o-tolyl), HCl 188° (decomposition); 1-[2-(1-carbethoxy-5-methylpyrazol-4 - ylcarbonyl)ethyl] - 4 - phenyl - 3 - methylpiperazine, -; 1-[2-(1-carbethoxy-5-methylpyrazol - 4 - ylcarbonyl)-ethyl)-4-(p-fluorophenyl)-3-methyl - 1,4 - diazacycloheptane, -. Also prepared, according to known methods, are the following N-(R-substituted)-4-(o-chlorophenyl)piperazines (R and salt m.p. given): 3 - hydroxy - 3 - (1 - carbethoxy - 5 - methylpyrazol-4-yl)propyl, 2HCl 175° (decomposition); 3-ethoxy-3-(1-carbethoxy-5-methylpyrazol-4-yl)propyl, maleate monohydrate 155-6°; 3-(1-carbethoxy-5-methylpyrazol-4-yl)allyl, -; 3-(1-carbethoxy-5-methylpyrazol-4-yl)propyl, maleate 120-2°; 3-acetoxy-3-(1-carbethoxy-5-methylpyrazol-4-yl)propyl, HCl, -; and (m.p. given): II, 67° (thiosemicarbazone m. 212°, guanylhydrazone-HCl m. 206°); 4-benzoyl-1-carbethoxy-5-methylpyrazole, 79-82°.
IT 21635-26-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 21635-26-7 CAPLUS
CN Pyrazole-1-carboxylic acid, 5-methyl-4-[3-(3-methyl-4-phenyl-1-piperazinyl)propionyl]-, ethyl ester (8Cl) (CA INDEX NAME)



L9 ANSWER 109 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1968:443935 CAPLUS
DOCUMENT NUMBER: 69:43935
TITLE: 1-(2-Ethoxy-2-phenylethyl)-4-arylpiperazines
INVENTOR(S): De Stevens, George; Mull, Robert P.
PATENT ASSIGNEE(S): CIBA Ltd.
SOURCE: Patentschrift (Switz.), 3 pp.
CODEN: SWXXAS
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

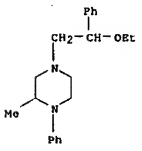
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| CH 446350 | | 19680315 | CH 1964-5558 | 19640120 <-- |

GI For diagram(s), see printed CA Issue.
AB 2-MeOC6H4NH(CH2)2NH2 (69 g.) and 9.2 g. EtOCHPhCH2Cl in 250 ml. was refluxed 24 hrs. to give 2-MeOC6H4NH(CH2)2NHCH2CH(OEt)Ph, which (5 g.) in 40 ml. BuOH was refluxed 17 hrs. with 3 g. (CH2Br)2 and excess Na2CO3 to give 1-(2-ethoxy-2-phenylethyl)-4-(2-methoxyphenyl)piperazine (I) (R = 2-MeOC6H4, R1 = H); di-HCl salt m. 215-17° (EtOH-MeCN). Similarly prepared were the following I (R, R1, b.p./mm., salt, and m.p. salt given): Ph, H, 177-80°/0.35, di-HCl, 225-8°; 2-ClC6H4, H, 200-5°/0.55, HCl, 200-3° (EtOAc); Ph, Me, 165-80°/0.5, di-HCl, 230-5° (EtOH); 3-MeC6H4, H, 185-90°/0.2, di-HCl, 197-9° (EtOH); and 2-pyridyl, H, 185-90°/0.5, di-HCl, 125-30° (EtOH-Et2O). I show

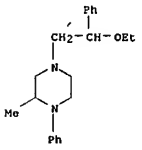




antiinflammatory, antihypertensive, adrenolytic, diuretic, and saliuretic activity and are norepinephrine antagonists.
IT 853-91-8P 853-92-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 853-91-8 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 853-92-9 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



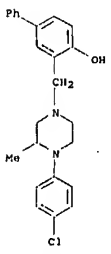
●2 HCl

L9 ANSWER 110 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1968:2801 CAPLUS
DOCUMENT NUMBER: 68:2801
TITLE: Potential anti-infective agents. I. Quinoline, phenolic, and β-aminoketone derivatives
AUTHOR(S): Magarian, Robert A.; Nobles, W. Lewis
CORPORATE SOURCE: Univ. of Mississippi, University, MS, USA
SOURCE: Journal of Pharmaceutical Sciences (1967), 56(8), 987-92
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.

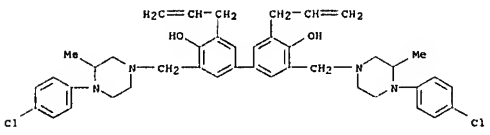




AB Mannich bases (e.g. I and II) were prepared, from quinolinols, isoquinolinols, phenols, biphenols, and ketones. Their antibacterial properties were evaluated. 25 references.
IT 16387-94-3P 16403-72-8P 16403-77-3P
16403-78-4P 16470-78-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 16387-94-3 CAPLUS
CN 4-Biphenylol, 3-[[4-(p-chlorophenyl)-3-methyl-1-piperazinyl]methyl]- (8CI) (CA INDEX NAME)



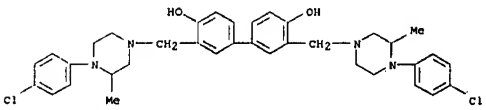
RN 16403-72-8 CAPLUS
CN [m,m'-Bitolyl]-4,4'-diol, 5,5'-diallyl-α,α'-bis[4-(p-chlorophenyl)-3-methyl-1-piperazinyl]- (8CI) (CA INDEX NAME)



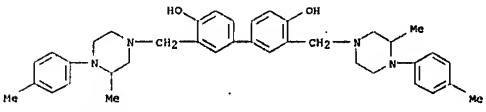
RN 16403-77-3 CAPLUS
CN [m,m'-Bitolyl]-4,4'-diol, α,α'-bis[4-(p-chlorophenyl)-3-methyl-1-piperazinyl]- (8CI) (CA INDEX NAME)





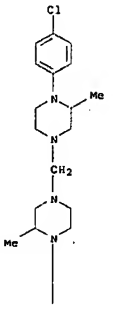


RN 16403-78-4 CAPLUS
CN [m,m'-Bitolyl]-4,4'-diol, α,α'-bis(3-methyl-4-p-tolyl-1-piperazinyl)- (8CI) (CA INDEX NAME)



RN 16470-78-3 CAPLUS
CN Piperazine, 1,1'-methylenebis[4-(p-chlorophenyl)-3-methyl- (8CI) (CA INDEX NAME)

PAGE 1-A



L9 ANSWER 111 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:104296 CAPLUS
DOCUMENT NUMBER: 64:104296
ORIGINAL REFERENCE NO.: 64:19641a-h,19642a
TITLE: Diazacycloalkanes
INVENTOR(S): Yost, William L.; Margerison, Richard B.
PATENT ASSIGNEE(S): CIBA Corp.
SOURCE: 10 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 3247206 | | 19660419 | US 1962-228760 | 19621005 <-- |
| PRIORITY APPLN. INFO.: | | | US | 19621005 |

GI For diagram(s), see printed CA Issue.
AB I-V, which can easily be prepared from R2R3CO, R1NH2, NaCN, and ClCHR4COCl, are treated with LiAlH4 to give VI-X. Similarly prepared are the correaponding diazacycloheptanes and diazacyclooctanes. To a solution of 830 g. NaHSO3 in 1540 ml. H2O was added during 1 hr. at 60-70° 352 g. AcH and, after 0.5 hr. stirring, 745 g. PhNH2 during 0.5 hr. Diluting with 200 ml. H2O, stirring 20 min., addg. 405 g. NaCN in 900 ml. H2O during 15 min. (temperature below 70°), and stirring 20 min. gave 61.5% N-(1-cyanoethyl)aniline (XI). To a mixture of 17.4 g. XI and 12.6 g. Na2CO3 in 87 ml. C6H6 was added 18.2 g. ClCH2COCl in 87 ml. C6H6 and the mixture refluxed 75 min. and kept overnight to give 95.7% I, m. 66-8°. A mixture of 11.37 g. LiAlH4 and 280 ml. tetrahydrofuran (THF) was refluxed under N 20 min. and cooled to 25°. After dropwise addition at 25° of 22.26 g. I in 85 ml. THF (18 min.), THF was distilled and replaced by PhMe, until during 50 min. 500 ml. distillate were collected. The mixture was refluxed 6 hrs., cooled to 25°, and quenched with 18 ml. H2O and 12.3 ml. 15% NaOH. After standing overnight, filtration, and evaporation, the residue was refluxed 2.5 hrs. with 8.5 g. Na2CO3 in 50 ml. PhMe to give 58.5% VI, b1 115-25°. Reaction of VI with an equimolar amount of PhNCS gave the phenylthiocarbamoyl derivative of VI, m. 158-60° (EtOH). A similar reduction of 222.6 g. I with 113.7 g. LiAlH4 led to 50% VI, b1 115-19°. Alternately, a mixture of 9.48 g. LiAlH4 and 22.26 g. I in 365 ml. THF was distilled and the THF replaced by xylene, until 340 ml. distillate was collected. The mixture was refluxed 6.75 hrs., cooled, treated with 15 ml. H2O and 10.25 ml. 15% NaOH, filtered, and evaporated. Refluxing the residue 2.5 hrs. with 8.5 g. Na2CO3 in 35 ml. PhMe gave 63.4% VI, b1 114-20°. To a suspension of 52.2 g. XI and 37.8 g. Na2CO3 in 482 ml. C6H6 was added dropwise during 10 min. 49.5 g. MeCHClCOCl in 100 ml. C6H6. The mixture was refluxed 2.5 hrs. and kept at room temperature overnight to give 70.4% II, m. 83-6°. Reduction of 23.65 g.





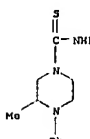
II with 11.37 g. LiAlH4 yielded 57.4% VII, b1. 117-25°, phenylthiocarbamoyl derivative m. 163-5° (EtOH). A mixture of 312.2 g. NaHSO3, 590 ml. H2O, and 43.5 g. Me2CO, prepared at 60-70°, was refluxed 45 min. and treated at 95° with 46.5 g. PhNH2. After 1 hr. reflux and addition of 100 ml. Me2CO and 29.5 g. NaCN in 65 ml. H2O, refluxing was continued 30 min. to give 68.8 g. N-(2-cyano-2-propyl)aniline (XII), m. 92-4° (50% EtOH). Refluxing 19.2 g. XII and 14.8 g. ClCH2COCl in C6H6 with Na2CO3 yielded III, m. 88-90° (AcOEt), which was dissolved in 85 ml. THF and added dropwise to 12 g. LiAlH4 in 300 ml. THF. The mixture was refluxed 6 hrs., quenched with 19 ml. H2O and 13 ml. 15% NaOH, filtered, and evaporated. The residue was refluxed 2.5 hrs. with Na2CO3 in PhMe to give 3.7 g. VIII, b1 110-15°; phenylthiocarbamyl derivative m. 193-5°. Refluxing a mixture of 29.2 g. XI and 27.7 g. Cl(CH2)2COCl 45 min. in C6H6 with 21.2 g. Na2CO3 gave crude N-(β-chloropropionyl)-N-(1-cyanomethyl)aniline (XIII), which was treated with 10.9 g. LiAlH4 in 385 ml. THF (6 hrs. reflux). Addition of 17.3 ml. H2O and 11.8 ml. 15% NaOH, filtration, evaporation, treatment of the residue with Na2CO3 in refluxing PhMe, and distillation gave 4.6 g. 2-methyl-1-phenyl-1,4-diazacycloheptane (XIV), b1 130-2°. Similarly, a solution of 34.2 g. XIII in 150 ml. THF was added to 16.15 g. LiAlH4 in 400 ml. THF at 37-40° and the mixture kept 2.5 hrs. to give 33.9% (based on XI) XIV, b1 118-20°. In this case, XIII was prepared from 29.2 g. XI, 27.7 g. Cl(CH2)2COCl, and 21.2 g. Na2CO3 in 350 ml. (ClCH2)2 by stirring 2.5 hrs. at -15° and keeping 16.5 hrs. at -35 to -40° to give a yield of 56.6 g. A mixture of 29.2 g. XI, 30 g. Cl(CH2)3COCl, and 21.2 g. Na2CO3 was refluxed 45 min. in C6H6 to give crude N-(γ-chlorobutyryl)-N-(1-cyanoethyl)aniline, which was treated with 10.9 g. LiAlH4 in 185 ml. THF (6 hrs. reflux) to give 10.4 g. 2-methyl-1-phenyl-1,4-diazacyclooctane, b1 138-42°. The reaction of paraformaldehyde with PhNH2 and HCN and treatment of the N-cyanomethylaniline with ClCH2COCl led to IV, which was treated with 3 equivs. LiAlH4 to give IX, b6 156°. Similarly, paraformaldehyde, iso-PrNH2, and KCN gave N-cyanomethyl-N-isopropylamine, which was treated with ClCH2COCl to give V. Reduction of V with 3 equivs. LiAlH4 furnished X, b. 156-63°. Reaction of H2C:CHCN with MeNH2 in the presence of a little PhCH2NMe3OH gave N-(2-cyanoethyl)-N-methylamine (XV), which was treated with ClCH2COCl. Reduction of the condensation product with LiAlH4 led to 1-methyl-1,4-diazacycloheptane, b32 71-3°. By reaction of XV with Cl(CH2)COCl and reduction of the condensation product with 3 equivs. LiAlH4 1-methyl-1,5-diazacyclooctane, b12 72-5°, was obtained. The new diazacycloalkanes are useful as anthelmintics and as intermediates for pharmaceuticals and germicides.
IT 2946-76-1P, Piperazine, 2-methyl-1-phenyl- 4318-46-1P, 1-Piperazinecarboxanilide, 3-methyl-4-phenylthio-
RL: PREP (Preparation)
(preparation of)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 4318-46-1 CAPLUS





CN 1-Piperazinecarboxanilide, 3-methyl-4-phenylthio- (7CI, 8CI) (CA INDEX NAME)



L9 ANSWER 112 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:59736 CAPLUS
DOCUMENT NUMBER: 64:59736
ORIGINAL REFERENCE NO.: 64:11149g-h,11150a-e
TITLE: 1,3-Cycloadditions of azomethinylides from aziridinecarboxylic esters
AUTHOR(S): Huisgen, Rolf; Scheer, Wolfgang; Szeimies, Guenter; Huber, Helmut
CORPORATE SOURCE: Univ. Munich, Germany
SOURCE: Tetrahedron Letters (1966), (4), 397-404
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: German
GI For diagram(s), see printed CA Issue.
AB cf. Heine and Peavy, CA 63, 14796e. By a ring opening between the 2 and 3 positions, di-Me 1-(p-methoxyphenyl)aziridine-2,3-dicarboxylate (I) adds to C:C and C.tplbond.C compds. to give pyrrolidine or pyrroline derivs. Heating di-Me 1-(p-methoxyphenyl)-Δ2-1,2,3-triazoline-4,5-trans-dicarboxylate at 100° gives I as a 15:85 cis-trans mixture. The reactions and epimerizations of I presumably proceed through the intermediate formation of epimers of MeO2CCH:N+(p-MeOC6H4)C-HCO2Me. Heating di-Me fumarate (II) and I at 140° yields 94% tetra-Me 1(p-methoxyphenyl)pyrrolidine-2,3,4,5-tetracarboxylate (III)containing an oily isomer (IIIa) and 59% of a crystalline isomer (IIIb), m. 112-13°. IIIa and IIIb are dehydrogenated by chloranil (IV) in boiling Decalin to give 21 and 22% yields, resp., of tetra-Me 1-(p-methoxyphenyl)pyrrole-2,3,4,5-tetracarboxylate, independently synthesized by the method of Huntress, et al. (CA 50, 12977b) from p-MeOC6H4NHOH and (MeO2CC.tplbond.)2. III is also prepared in 61% yield from II and p-MeOC6H4N3 at 100-140°. At 120°, I and [(EtO2C)2CH-]2 give 77% of 2,5-di-Me 3,3,4,4-tetra-Et 1-(p-methoxyphenyl)pyrrolidine-2,3,3,4,4,5-hexacarboxylate containing 65% of the cis form, m. 114-15°, and 35% of the trans form, m. 114-16°, separated on silica gel by 9:1 C6H6-Et2O. The addition of norbornene to I at 100° gives 94% V containing 63% cis form (V, R = CO2Me, R1 = H), an oil, and 37% trans form (V, R = H, R1 = CO2Me), m. 87-9°, separated by thin layer chromatography. IV in boiling cymene converts V to VI, m. 161-2°. At 125°, I combines with HC.tplbond.CH in Me2CO to give an 81% yield of adducts, presumably a mixture of Δ2- and Δ3-pyrrolines which are dehydrogenated by IV in boiling xylene to give a 68% yield of di-Me 1-(p-methoxyphenyl)pyrrole-2,5-dicarboxylate, identical to the product obtained from p-MeOC6H4NH2 and

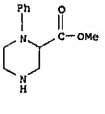




di-Me α,α'-dihydroxymuconate (Kuhn and Dury, CA 45, 7017a). BzC.tplbond.CPh and I at 100° yield 93% of an adduct dehydrogenated by IV in PhMe to give 55% di-Me ester of 3-benzoyl-1-(p-methoxyphenyl)-4-phenylpyrrole-2,5-dicarboxylic acid (VII). VII decarboxylates at 200° to give 3-benzoyl-1-(4-methoxyphenyl)-4-phenylpyrrole (VIII), characterized by its 2,4-dinitrophenylhydrazone. VIII is also prepared by condensing the Na derivative of BzCH2CHO with p-MeOC6H4NHCH2Br, and cyclizing the product with concentrated H2SO4. Photochem. or thermally (150°), I dimerizes to give a mixture from which two isomers, m. 188-9° and 240-1°, of tetra-Me 1,4-bis(p-methoxyphenyl)piperazine-2,3,5,6-tetracarboxylate have been isolated. Heating Me 1-phenylaziridine-2-carboxylate (IX) 6 hrs. at 200° gave 50% of the di-Me ester of 1,4-diphenylpiperazine-2,3-trans-dicarboxylic acid (X), m. 132-3°, and 5% of the cis ester, m. 105-6°. Distillation of Ca salt of X yields (PhNHCH2)2 and 1,4-diphenylpiperazine. The reaction of IX with trans-(BzCH:)2 (XI) gives a 1:1 adduct, m. 120-1°, and with PhCH:NMe, an adduct, m. 132.5-4° (structures not given). The addition of 1-benzyl-2,3-trans-dibenzoylaziridine to XI gives 34% of 1-benzyl-2,3,4,5-(all-trans)-tetrabenzoylpyrrolidine.
IT 5969-86-8P, Methylamine, N-benzylidene-, compound with Me 1-phenyl-2-aziridinecarboxylate (1:1)
RL: PREP (Preparation)
(preparation of)
RN 5969-86-8 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-phenyl-, methyl ester, compd. with N-benzylidenemethylamine (1:1) (8CI) (CA INDEX NAME)

CM 1

CRN 46490-35-1
CMF C12 H16 N2 O2



CM 2

CRN 622-29-7
CMF C8 H9 N

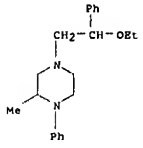


L9 ANSWER 113 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:416903 CAPLUS
DOCUMENT NUMBER: 63:16903
ORIGINAL REFERENCE NO.: 63:2985g-h
TITLE: 1-(2-Phenyl-2-ethoxyethyl)-4-phenylpiperazines
INVENTOR(S): De Stevens, George; Mull, Robert P.

PATENT ASSIGNEE(S): CIBA Ltd.
SOURCE: 32 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| BE 642845 | | 19640722 | BE | | <-- |
| FR 1404442 | | | FR | | |
| FR M3308 | | | FR | | |
| FR M3309 | | | FR | | |
| GB 1047044 | | | GB | | |
| PRIORITY APPLN. INFO.: | | | US | 19630123 | |

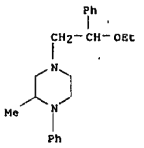
OTHER SOURCE(S): MARPAT 63:16903
GI For diagram(s), see printed CA Issue.
AB Compds. of the general formula I are prepared and can be used as antiinflammatory and diuretic agents.. Thus, a mixture of 11.8 g. Ph(EtO)CHCH2Cl, 12.5 g. 1-(2-methoxyphenyl)piperazine, and 200 ml. BuOH is refluxed 24 hrs. in the presence of 40.0 g. Na2CO3 to give 1-(2-ethoxy-2-phenylethyl)-4-(2-methoxyphenyl)piperazine, b0.9 179-80°, 2HCl salt m. 215-17° (EtOH and MeCN). Also prepared are the following I (R, X, Y, b.p./mm., and m.p. 2HCl salt given): H, H, H, 177-80°/0.35, 225-8°; H, Cl, H, 200-5°/0.55, 200-3° (EtOAc); Me, H, H, 165-80°/0.5, 230-5° (EtOH); H, H, Me, 185-90°/0.2, 197-9° (EtOH). Also prepared are 1-(2-ethoxy-2-phenylethyl)-4-(2-pyridyl)piperazine (b0.5 185-90°, 2HCl salt m. 125-30° (EtOH and Et2O)), 1-(2-hydroxy-2-phenylethyl)-4-(2-methoxyphenyl)piperazine, (Cl CH2CH2)2NCH2CH(OEt)Ph.
IT 853-91-8P, Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl- 853-92-9P, Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride
RL: PREP (Preparation)
(preparation of)
RN 853-91-8 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 853-92-9 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)





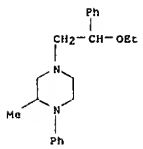


●2 HCl

L9 ANSWER 114 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:85303 CAPLUS
DOCUMENT NUMBER: 62:85303
ORIGINAL REFERENCE NO.: 62:15243g-h
TITLE: Anesthetic effect of some variants of mepivacaine (carbocaine). Preliminary studies and clinical impressions
AUTHOR(S): Feldmann, Gunter; Nordenram, Ake
CORPORATE SOURCE: Central Hosp., Karlstad, Swed.
SOURCE: J. Oral Therap. Pharmacol. (1965), 1(4), 421-7
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Carbocaine I (R = Me, R' = H) was clinically tested with analogs (Ekenstam, CA 52, 14609e) for local anesthetic activity. I (R = Et, R' = H) and I (R = H, R' = Me) were longer lasting than carbocaine, though the time of onset was somewhat longer.
IT 853-92-9P, Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride 905-90-8P, Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride 1168-17-8P, Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl-, dihydrochloride 2281-97-2P, Piperazine, 4-(3-methoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride
RL: PREP (Preparation)
(preparation of)
RN 853-92-9 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)

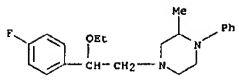






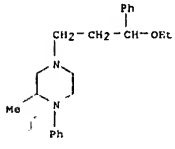
●2 HCl

RN 905-90-8 CAPLUS
CN Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



●2 HCl

RN 1168-17-8 CAPLUS
CN Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)

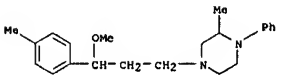


●2 HCl

RN 2281-97-2 CAPLUS
CN Piperazine, 4-(3-methoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)

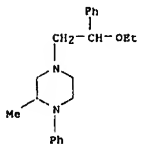






●2 HCl

L9 ANSWER 115 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:85302 CAPLUS
DOCUMENT NUMBER: 62:85302
ORIGINAL REFERENCE NO.: 62:15243f-g
TITLE: N,N'-Disubstituted compounds with diverse biological activities
AUTHOR(S): Mull, Robert P.; Tannenbaum, Carl; Dapero, Mary R.; Bernier, Marcel; Yost, William; De Stevens, George
CORPORATE SOURCE: CIBA Corp., Summit, NJ
SOURCE: Journal of Medicinal Chemistry (1965), 8(3), 332-8
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A large number of N,N'-disubstituted compds. were prepared for broad biol. testing. Some N-phenylpiperazine derivs. had antihypertensive, adrenolytic, and antiinflammatory properties. A structure-activity relation study was carried out to sep. these activities in single compds.
IT 853-92-9P, Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride 905-90-8P, Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride 1168-17-8P, Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl-, dihydrochloride 2281-97-2P, Piperazine, 4-(3-methoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride 2946-76-1P, Piperazine, 2-methyl-1-phenyl-
RL: PREP (Preparation)
(preparation of)
RN 853-92-9 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



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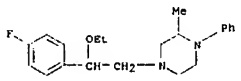
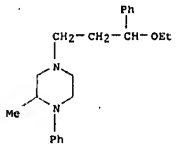
RN 905-90-8 CAPLUS
CN Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



●2 HCl

RN 1168-17-8 CAPLUS
CN Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)

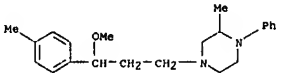


●2 HCl

RN 2281-97-2 CAPLUS
CN Piperazine, 4-(3-methoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)







●2 HCl

RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

L9 ANSWER 116 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:85301 CAPLUS
DOCUMENT NUMBER: 62:85301
ORIGINAL REFERENCE NO.: 62:15243e-f
TITLE: Structure-activity relations in the field of antibacterial steroid acids
AUTHOR(S): Fried, Josef; Krakower, Gerald W.; Rosenthal, David; Basch, Harold
CORPORATE SOURCE: Squibb Inst. for Med. Res., New Brunswick, NJ
SOURCE: Journal of Medicinal Chemistry (1965), 8(3), 279-82
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antibacterial activity of a variety of steroidal and triterpenoid acids was determined using Staphylococcus aureus 209P as the test organism. Activity was less dependent on specific structural and stereo-chemical features than had been anticipated. All active compds. have a rigid polycyclic skeleton with a carboxyl group close to an O function or a double bond.
IT 2946-76-1P, Piperazine, 2-methyl-1-phenyl-
RL: PREP (Preparation)
(preparation of)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)





L9 ANSWER 117 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:74269 CAPLUS
DOCUMENT NUMBER: 62:74269
ORIGINAL REFERENCE NO.: 62:13159h,13160a-d
TITLE: Cyclic diaza compounds
INVENTOR(S): Yost, William L.; Margerison, Richard B.
PATENT ASSIGNEE(S): CIBA Ltd.
SOURCE: 48 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| FR 1378964 | | 19641120 | FR 1963-949434 | 19631003 <-- |
| GB 1041086 | | | GB | |
| PRIORITY APPLN. INFO.: | | | US | 19621005 |

AB Compds. of the general formula X(CH2)nNR(CH2)mCN, in which X is halogen, m and n may be 1 or 2, and some or all C atoms may have alkyl or other groups, are cyclized by reduction with LiAlH4 or similar agents, hydrolysis, and heating with alkali. A solution of 11.37 g. LiAlH4 in 280 ml. tetrahydrofuran was added dropwise at 25° to 22.26 g. PhN(COCH2Cl)CHMeCN (I) in 85 ml. tetrahydrofuran. After the initial reaction subsided the solvent was distilled, and replaced by toluene. Distillation was continued at such a rate that 500 ml. total distillate was collected in 50 min. and pot temperature was 110°. After 6 hrs. addnl. heating the mixture was cooled and poured into 15% NaOH solution. After several hrs. the organic layer was washed and evaporated to dryness. The product was then refluxed in 50 ml. toluene with 8.5 g. Na2CO3 2 hrs., the solvent evaporated, and the 2-methyl-1-phenylpiperazine was distilled, b1 115-25°; 4-phenylthiocarbamatem. 158-60°(alc.). Aniline(745 g.) was slowly added at 60-70° to a solution of addition product of 352 g. AcH and 830 g. NaHSO3 in 1540 ml. water. The mixture was diluted with 200 ml. water and a solution of 405 g. NaCN in 900 ml. water was added in 15 min. The mixture was stirred 20 min., cooled to 10° and filtered and H2O added to give N-(1-cyanoethyl)aniline (II), m. 90-2° (alc.). A solution of 18.2 g. ClCH2COCl in 87 ml. benzene was slowly added to a mixture of 17.4 g. II in 87 ml. benzene and 12.6 g. Na2CO3. The mixture was boiled 75 min. and cooled, and after several hrs., filtered and evaporated. The residue was dissolved in 200 ml. 50% aqueous alc. and cooled to -8° to give I, m. 66-8°. Similarly prepared were: 2,5-dimethyl-1-phenylpiperazine, b1 117-25° [phenylthiocarbamate m. 163-5° (alc.)], and the following piperazines (substituents given): 2,2-dimethyl-1-phenyl, b1, 110-15° [phenylthiocarbamate m. 193-5° (alc.)]; 1-isopropyl, b. 156-63°. Anilines prepared were (substituents given): N-(α-chloropropionyl)-N-(1-cyanoethyl), m. 83-6° (anhydrous EtOH); N-(2-cyano-2-propyl), m. 88-90° (EtOAc); N-(β-chloropropionyl)-N-(cyanoethyl). Other compds. prepared were: 2-methyl-1-phenyl-1,4-diazacycloheptane, b1 130-2°; 2-methyl-1-phenyl-1,4-diazacyclooctane, b1 138-42°; 1-methyl-1,4-diazacycloheptane, b32 71-3°; 1-methyl-1,5-diazacyclooctane, b12 72-5°, [di-HBr salt m. 215-17° (alc.)]. Some of these compds. are useful as anthelmintic, germicidal, or adrenolytic agents. They are also accelerators for rubber mfg.

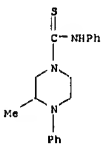
IT 2946-76-1P, Piperazine, 2-methyl-1-phenyl- 4318-46-1P, 1-Piperazinecarboxanilide, 3-methyl-4-phenylthio-





RL: PREP (Preparation)
(preparation of)
RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 4318-46-1 CAPLUS
CN 1-Piperazinecarboxanilide, 3-methyl-4-phenylthio- (7CI, 8CI) (CA INDEX NAME)



L9 ANSWER 118 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:66601 CAPLUS
DOCUMENT NUMBER: 62:66601
ORIGINAL REFERENCE NO.: 62:11833a-d
TITLE: Substituted piperazines
INVENTOR(S): de Steven, George; Mull, Robert P.
PATENT ASSIGNEE(S): Ciba Soc.
SOURCE: 34 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| FR 1382425 | | 19641218 | FR 1964-959909 | 19640110 <-- |
| BE 642429 | | | BE | |
| PRIORITY APPLN. INFO.: | | | US | 19630114 |

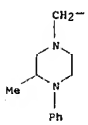
AB 3-Methyl 4-phenyl-1-(2-phenylthioethyl)piperazine di-HCl salt, m. 214-15° (EtOH-Et2O), was prepared by refluxing 7.04 g. 2-methyl-1-phenylpiperazine and 4.34 g. PhS(CH2)2Br in 75 cc. PhMe 6 hrs. Similarly were prepared 4-(2-methoxyphenyl)-1-(2-phenylthioethyl)piperazine di-HCl salt, m. 190-3° (PhMe-EtOH), 4-(2-methoxyphenyl)-1-[2-(4-tert-butylphenylthio)ethyl]-piperazine di-HCl salt, m. 200-5° (PhMe-EtOH), and 1-[2-(2-isopropylphenylthio)ethyl]-4-(2-methoxyphenyl)piperazine di-HCl salt, m. 200-5° (PhMe-EtOH). 4-Phenyl-1-(2-phenylthio-ethyl)piperazine di-HCl salt (I), m.

198-9° (EtOH) (free base b0.6 190-200°) was prepared by refluxing 5 g. PhS(CH2)2Br and 4.35 g. 1-phenylpiperazine in 200 cc. BuOH containing 10 drops H2O and 6 g. Na2CO3 92 hrs. [ was also prepared by refluxing 7.65 g. PhS(CH2)2NH2 (II), 10.9 g. PhN[(CH2)2Cl]2 in 50 cc. MeOH, and excess K2CO3 15 hrs., or similarly using N,N-bis(2-chloro-ethyl)-N-(2-phenylthioethyl)amine (III) and 10 g. PhNH2. 2-(4-tert-Butylphenylthio)ethyl bromide, m. 176-7°, was prepared by adding 35.6 g. Cl(CH2)2OH to 55 g. 4-tert-butylthiophenol in 132 cc. 10% NaOH, stirring the solution 1 hr. at room temperature, and refluxing the mixture 30 min. to give 2-(4-tert-butylphenylthio)-ethanol b12 175-6° which (21 g.) was added dropwise to 10.84 g. PBr3 and 3 g. pyridine at 0° and stirred overnight. II was prepared by refluxing 46 g. PhS(CH2)2Br, 44 g. K phthalimide, and a few crysts. iodine in 80 cc. HCONHMe2 2 hrs., refluxing the crude product 2 hrs. with 20 g. N2H4 in 200 cc. MeOH, cooling, acidifying the solution with HCl, and refluxing 30 min. III was prepared by heating for 16 hrs. in a sealed tube 15.3 g. PhS(CH2)2NH2 and 9 g. (CH2)2O and adding 23.5 g. of the obtained N,N-bis(2-hydroxyethyl)-N-(2-phenylthioethyl)amine with cooling to 25 g. PCl5 in 100 cc. dry CHCl3 and refluxing the mixture 2-(2-Isopropylphenylthio)ethyl bromide, b12 157-8°, was prepared from 2-isopropylthiophenol and HOCH2CH2Cl and the product, 2-(2-isopropylphenylthio)ethanol, b1 130-5°, treated with PBr3 and C5H5N. The title compds, are antihypertensive and antiinflammatory agents.

IT 1039-99-2P, Piperazine, 2-methyl-1-phenyl-4-[2-(phenylthio)ethyl]-, dihydrochloride
RL: PREP (Preparation)
(preparation of)

RN 1039-99-2 CAPLUS

CN Piperazine, 2-methyl-1-phenyl-4-[2-(phenylthio)ethyl]-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



●2 HCl

L9 ANSWER 119 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:66597 CAPLUS
DOCUMENT NUMBER: 62:66597
ORIGINAL REFERENCE NO.: 62:11831c-h,11832a-d
TITLE: N-Aryl-N'-aralkyldiazacycloalkanes
INVENTOR(S): De Stevens, George; Mull, Robert P.
PATENT ASSIGNEE(S): CIBA Corp.
SOURCE: 14 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable





FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 3168522 | | 19650202 | US 1963-315405 | 19631010 <-- |
| PRIORITY APPLN. INFO.: | | | US | 19631010 |

GI For diagram(s), see printed CA Issue.

AB The title compds. (I) have adrenolytic, antihypertensive, antiinflammatory, diuretic, saluretic, analgesic, and antifibrillatory properties. To a solution of 8.8 g. 2-methyl-1-phenylpiperazine in 50 ml. toluene was added 2.4 g. of a mineral oil suspension (53%) of NaH. The mixture was refluxed 2 hrs. and then refluxed overnight with 11.6 g. 3-ethoxy-3-(4-methylphenyl)propyl chloride. After filtering off inorg. material, the filtrate was distilled to yield 1-[3-ethoxy-3-(4-methylphenyl)propyl]-3-methyl-4-phenylpiperazine, b0.2 182-4°; dihydrochloride m. 190-2°. In this manner were prepared the I (n = 2) given in the first table. Crude 3-(4chlorophenyl)-3-ethoxypropylamine (II) was prepared from 50 g. 3-(4-chlorophenyl)-3-ethoxypropyl chloride and 44 g. K phthalimide in 80 ml. dimethylformamide. m.p., R, R1, R2, R3, b.p./mm., m.p. di-HCl salt, Et, H, Me, H, 168-70°/0.075, 194°; iso-Pr, 4-Me, Me, H, 146-54°/0.04, 169°; Me, 4-Me, H, H, 170-2°/0.05, 200°; Et, 4-Me, H, H, 196°/0.04, 194°; Et, 4-Me, H, 3-Me, 172-4°/0.04, 165°; Me, 4-Me, Me, H, 176-8°/0.1, 197-8°; Me, 4-Me, H, 2-Me, 180-2°/0.12, 163°; Me, 4-Me, H, 2-Cl, 182-4°/0.05, 153-5°; Me, 4-Me, H, 3-Me, 174-8°/0.07, 155°; iso-Pr, 4-Me, H, 2-Me, 176-80°/0.04, 171-3°; iso-Pr, 4-Me, H, 2-Cl, 194-200°/0.04, 159°; iso-Pr, 4-Me, H, 4-Me, 190-2°/0.09, 173°; Et, H, H, 2-Cl, 176-8°/0.03, 141-3°; Me, 4-Me, H, 4-Me, 208-12°/0.09, 192°; Et, H, H, 4-Cl, 238-40°/0.08, 155°; Et, H, H, 2-Me, 180-2°/0-2, 150-4°; Et, H, H, 4-Me, 180-3°/0.2, 200°; Et, H, H, 4-OMe, --, 210-11°; Et, H, H, H, 160°/0.15, 202-3°; Et, 4-Cl, H, H, 168°/0.1, 208°; Et, 4-Cl, Me, H, 206-8°/0.07, 192°; Et, 4-Me, H, H, 186°/0.05, 164-6°; Et, 4-Me, H, 2-Cl, 184-6°/0.04, 150-2°; Et, 4-Me, H, 2-Me, 222-4°/0.14, 186°; Et, 4-Me, H, 3-Cl, 208-10°/0.06, 168-70°; Me, 4-Me, H, 2-OMe, --, 175-7°; Et, 4-Cl, H, 4-Cl, 214-16°/0.11, 188°; Et, 4-Cl, H, 3-OMe, 204-6°/0.12, 165°; Me, 4-Cl, Me, H, 170-8°/0.05, 184°; Et, 4-Cl, H, 4-Me, 196-200°/0.04, 197°; iso-Pr, 4-Cl, H, H, 198-200°/0.09, 200°; Me, 4-Cl, H, H, 192-4°/0.08, 215°; Me, 4-Cl, H, 4-Me, 186-90°/0.09, 195°; Me, 4-Cl, H, 2-Me, 208-10°/0.17, 165°; Et, 4-Cl, H, 3-Me, 180-2°/0.04, 173°; Et, 4-Me, H, 4-Me, 192-6°/0.011, 194-5°; Et, 4-Me, H, 4-Cl, --, 174-6°; Et, 4-Cl, H, 2-Me, 198-202 °/0.16, 184°; Et, 4-Cl, H, 2-Cl, 210-12°/0.07, 120°; Et, 4-Cl, H, 3-Cl, 206-8°/0.06, 169°; Et, 2-Cl, H, H, 182-4°/0.08, 170°; Et, 4-Me, H, 2-Me, 186°/0.05, 164-6°; Et, H, H, 3-Me, 172-4°/0.05, 166°; Et, 4-Cl, H, 2-OMe, 206-10°/0.13, 200°; Et, H, H, 3-OMe, --, 163°; N,N-bis(2-chloroethyl)-N-(2-chlorophenyl)amine (III) was prepared by heating a mixture of 2-chloroaniline and ethylene oxide in a sealed tube and converting the resulting N-(2-chlorophenyl)-N,N-bis(2-hydroxyethyl)amine to III with SOCl2. A mixture of 21.3 g. II and 25.2 g. III in 100 ml. MeOH was refluxed with excess K2CO3 15 hrs. to give I. A mixture of 2490 g.





1-(2-methylphenyl)piperazine dihydrochloride, 285 g. paraformaldehyde, and 1735 g. 4-methylacetophenone in 7500 ml. EtOH was refluxed 24 hrs. with stirring and cooled to -10° and the precipitate filtered off and washed 3 times with 1000 ml. cold acetone to give 2850 g. 1-[3-(4-methylphenyl)-3-oxopropyl] -4-(2-methylphenyl)piperazine hy-drochloride (IV), m. 209-11°. Reduction of 2660 g. IV with 407 g. NaHB4 gave 2530 g. 1-[3-hydroxy-3-(4-methylphenyl)propyl]-4-(2-methylphenyl)piperazine (V), m. 80-3°. A solution of 2530 g. V in 19 ml. benzene was gassed with HCl to a pH of 2 and treated with 2750 g. SOCl2 in 12 ml. benzene, the mixture refluxed 2 hrs., and the remaining SOCl2 and benzene were distilled The residue in 12 ml. EtOH was held below 15° while adding 718 g. Na in 23 ml. EtOH and then refluxed 1 hr. The solution was evaporated to dryness and the residue dissolved in 80 ml. water and extracted with CHCl3 to yield 2700 g. 1-[3-ethoxy-3-(4-methylphenyl)propyl]-4-(2-methylphenyl)piperazine which gave a dihydrochloride m. 165-8°. The Grignard reagent from 76.4 g. 4-chlorobromo-benzene and 8.16 g. Mg condensed with 48.0 g. 1,2-dichlorodiethyl ether gave 2-(4-chlorophenyl)-2-ethoxyethyl chloride (VI), b12 122-40°. Condensation of VI with aryl piperazines by refluxing 24 hrs. in the presence of Na2CO3 gave I. In this manner were prepared I (n = 1), given in the second table. Also prepared R, R1, R2, R3, b.p./mm., m.p.di-HCl salt; Et, 4-Cl, H, 2-OMe, 190-200°/0.3, 229-31°; Et, 4-Cl, H, H , 90-1°/0. 3, 203-5°; Et, H, H, 2-OMe, 179-80°/0.9, 215-17°; Et, H, H, H, 177-80°/0. 35, 225-8°; Et, 3-CF3, H, H, 128-40°/0.35, 182-5°; Et, H, H, 2-Cl, 200-5°/0. 55, 200-3°; Et, H, Me, H, 165-80°/0.5, 230-5°; Et, 3,4-Cl2, H, 2-OMe, 210-20°/0.7, 221-5°; Et, 4-Cl, H, 2-Cl, 185-90°/0.2, 240-4°; Et, 3,4-Cl2, H, H, 210-20°/0.7, 211-13°; Et, 3-Cl, H, 2-OMe, 170-90°/0.7, 213-17°; Et, 3-Cl, H, H, 180-200°/0.7, 192-3°; Et, H, H, 3-Me, 185-90°/0.2, 197-9°; Et, 4-F, H, 3-Me, 160-85°/0.8, 193-60°; Et, 4-F, Me, H, 170-5°/0.6, 228-32°; Were the following VII (n, R, b.p./mm., and m.p. di-HCl salt given): 1, H, 185-90°/0.5, 125-30°; 2, 4-Me, 162-3°/0.25, 194-5°.

IT 442-26-2P, Piperazine, 4-(3-ethoxy-3-p-tolylpropyl)-2-methyl-1-phenyl- 745-59-5P, Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl- 745-60-8P, Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl- 748-03-8P, Piperazine, 4-(3-isopropoxy-3-p-tolylpropyl)-2-methyl-1-phenyl- 853-91-8P, Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl- 853-92-9P, Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride 905-90-8P, Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride 905-91-9P, Piperazine, 4-(3-methoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, hydrochloride 905-92-0P, Piperazine, 4-[3-(p-chlorophenyl)-3-methoxypropyl]-2-methyl-1-phenyl- 907-68-6P, Piperazine, 4-(3-ethoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride 978-11-0P, Piperazine, 4-[3-(p-chlorophenyl)-3-methoxypropyl]-2-methyl-1-phenyl-, dihydrochloride 1049-29-2P, Piperazine, 4-(3-methoxy-3-p-tolylpropyl)-2-methyl-1-phenyl- 1051-75-8P, Piperazine, 4-[3-(p-chlorophenyl)-3-ethoxypropyl]-2-methyl-1-phenyl- 1051-76-9P, Piperazine, 4-[3-(p-chlorophenyl)-3-ethoxypropyl]-2-methyl-1-phenyl-, dihydrochloride 1168-17-8P, Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl-, dihydrochloride 3792-38-9P, Piperazine, 4-(3-isopropoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride
RL: PREP (Preparation)

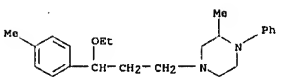




(preparation of)

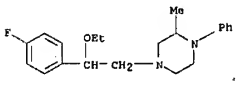
RN 442-26-2 CAPLUS

CN Piperazine, 4-[3-ethoxy-3-(4-methylphenyl)propyl]-2-methyl-1-phenyl- (9CI) (CA INDEX NAME)



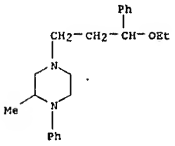
RN 745-59-5 CAPLUS

CN Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



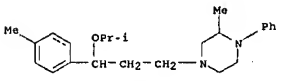
RN 745-60-8 CAPLUS

CN Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



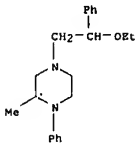
RN 748-03-8 CAPLUS

CN Piperazine, 4-(3-isopropoxy-3-p-tolylpropyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)

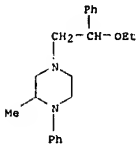


RN 853-91-8 CAPLUS

CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)

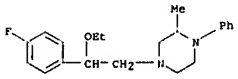


RN 853-92-9 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



●2 HCl

RN 905-90-8 CAPLUS
CN Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)

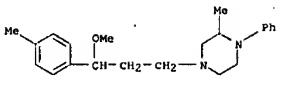


●2 HCl

RN 905-91-9 CAPLUS
CN Piperazine, 4-(3-methoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, hydrochloride (7CI, 8CI) (CA INDEX NAME)

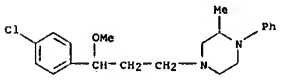






● HCl

RN 905-92-0 CAPLUS
CN Piperazine, 4-[3-(p-chlorophenyl)-3-methoxypropyl]-2-methyl-1-phenyl- (8CI) (CA INDEX NAME)



RN 907-68-6 CAPLUS
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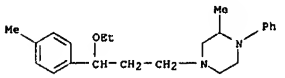
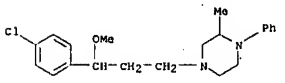


●2 HCl

RN 978-11-0 CAPLUS
CN Piperazine, 4-[3-(p-chlorophenyl)-3-methoxypropyl]-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)

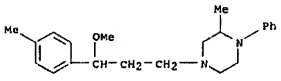


●2 HCl

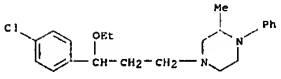




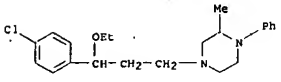
RN 1049-29-2 CAPLUS
CN Piperazine, 4-(3-methoxy-3-p-tolylpropyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 1051-75-8 CAPLUS
CN Piperazine, 4-[3-(p-chlorophenyl)-3-ethoxypropyl]-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 1051-76-9 CAPLUS
CN Piperazine, 4-[3-(p-chlorophenyl)-3-ethoxypropyl]-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)

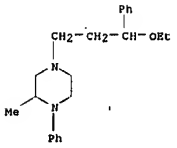


●2 HCl

RN 1168-17-8 CAPLUS
CN Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)

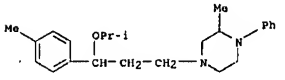






●2 HCl

RN 3792-38-9 CAPLUS
CN Piperazine, 4-(3-isopropoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



●2 HCl

L9 ANSWER 120 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:43961 CAPLUS
DOCUMENT NUMBER: 62:43961
ORIGINAL REFERENCE NO.: 62:7777f-h
TITLE: Piperazinoalkyl esters of 9-hydroxyfluorene-9-carboxylic acid
INVENTOR(S): Biel, John H.
PATENT ASSIGNEE(S): Colgate-Palmolive Co.
SOURCE: 3 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 3162637 | | 19641222 | US 1960-14502 | 19600314 <-- |
| PRIORITY APPLN. INFO.: | | | US | 19600314 |

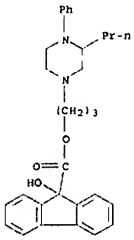
GI For diagram(s), see printed CA Issue.
AB The title compds. (I), in which Y is alkylene and R is alkyl or aryl, were made. Thus, a mixture of 21.7 g. Me 9-hydroxy-fluorene-9-carboxylate, 14.2 g. N-methyl-N1-(3-hydroxypropyl)-piperazine, 0.5 g. MeONa, and 250 cc. heptane was refluxed 6 hrs., during which time 5.3 cc. MeOH was collected. The catalyst was then filtered off and the filtrate washed by H2O to yield

33.1 g. I [Y = (CH2)3, R = Me]; di-HCl salt m. 237° (decomposition) (MeOH). Similarly prepared were I (Y, R, and m.p. of di-HCl salt given): MeCHCH2, Me, 234° (decomposition); MeCHCH2, Ph, 239° (decomposition) (II). These I have ataractic effects and induce mild muscle relaxation. II is an antispasmodic.

IT 1864-47-7P, Fluorene-9-carboxylic acid, 9-hydroxy-, 3-(4-phenyl-3-propyl-1-piperazinyl)propyl ester 2083-58-1P, Fluorene-9-carboxylic acid, 9-hydroxy-, 3-(4-phenyl-3-propyl-1-piperazinyl)propyl ester, dihydrochloride
RL: PREP (Preparation)
(preparation of)

RN 1864-47-7 CAPLUS

CN Fluorene-9-carboxylic acid, 9-hydroxy-, 3-(4-phenyl-3-propyl-1-piperazinyl)propyl ester (7CI, 8CI) (CA INDEX NAME)

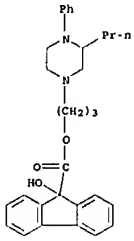


RN 2083-58-1 CAPLUS

CN Fluorene-9-carboxylic acid, 9-hydroxy-, 3-(4-phenyl-3-propyl-1-piperazinyl)propyl ester, dihydrochloride (7CI, 8CI) (CA INDEX NAME)







●2 HCl

L9 ANSWER 121 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:22615 CAPLUS
DOCUMENT NUMBER: 62:22615
ORIGINAL REFERENCE NO.: 62:4038g-h,4039a
TITLE: Piperazine-bithionol anthelmintic
INVENTOR(S): Gillingham, James M.; Clark, John C.
PATENT ASSIGNEE(S): Diamond Laboratories, Inc.
SOURCE: 2 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 3152041 | | 19641006 | US 1961-112533 | 19610525 <-- |
| PRIORITY APPLN. INFO.: | | | US | 19610525 |

GI For diagram(s), see printed CA Issue.

AB Piperazine-bithionol (piperazine-bithionolate) (I), m. 214-15°, having a wider spectrum of activity against parasitic infections in a large variety of animals than either of its precursors or salts is prepared from various ratios of piperazine (II) to bithionol (III) in acetone solution or precipitated from aqueous alkaline solution by acid. Thus, to 17.2 g. II anhydrous base in 250 ml. acetone was added 36.6 g. III in 250 ml. acetone in 5-ml. increments with mixing; crystals appeared at pH 10.5, and I crystallized at the end of the addition in 27-g. yield after separation and drying. It can be recrystd. from BuOH. In aqueous alkali, I had uv absorption values E1%1cm. maximum 236 at 327 mμ and min. 58 at 285 mμ. The L.D.50 (in mice) of I, II citrate, III, and II citrate-III is, resp.: 800, 4000, 3190, 1007 mg./kg. Two cats given 10 times the normal therapeutic dose of 150 mg./lb. I as an oral suspension showed no adverse effects, and 2 of 3 cats given 10 times the therapeutic dose in capsules showed only fecal softening and very slight tranquilization. I in doses of 150 mg./lb. for



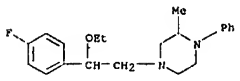


ascarid infection caused 100% egg reduction in dogs and 91% in cats; in one cat with hookworms the egg reduction was 70%.

IT 745-59-5P, Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl- 905-90-8P, Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride
RL: PREP (Preparation)
(preparation of)

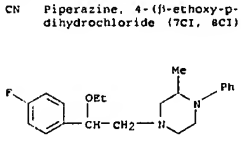
RN 745-59-5 CAPLUS

CN Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 905-90-8 CAPLUS

CN Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



●2 HCl

L9 ANSWER 122 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:22614 CAPLUS
DOCUMENT NUMBER: 62:22614
ORIGINAL REFERENCE NO.: 62:4038e-g
TITLE: Medicinal piperazine compounds
PATENT ASSIGNEE(S): CIBA Ltd.
SOURCE: 18 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| NL 6400467 | | 19640724 | NL 1964-467 | 19640122 <-- |
| BE 642844 | | | BE | |
| FR 1385772 | | | FR | |
| PRIORITY APPLN. INFO.: | | | US | 19630123 |

GI For diagram(s), see printed CA Issue.

AB The title compds. (I) show antipyretic, antiinflammatory, hypotensive, adrenolytic, and diuretic properties; they are norepinephrine antagonists.



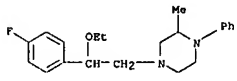


A mixture of 10.05 g. 1-(2-methoxyphenyl)piperazine, 11.5 g. 2-(4-chlorophenyl)-2-ethoxyethyl chloride (II), and 40.0 g. Na2CO3 in 200 ml. BuOH is refluxed 24 hrs. with stirring. After separation of the inorg. material, the filtrate is evaporated and the residue distilled to give I (X = 4-Cl, R2 = Et, R1 = H, Ar = 2-MeOC6H4), b0.3 190-200°; di-HCl salt m. 229-31° (iso-PrOH). II (b12 122-40°) is prepared by a Grignard reaction from 8.16 g. Mg in 75 ml. Et2O, 76.4 g. 4-ClC6H4Br, and 48 g. ClCH2CHClOEt. Similarly are prepared the following I (X, R2, R1, Ar, b.p./mm., and m.p. di-HCl salt listed): 4-Cl, Et, H, Ph, 90-1°/0.3, 203-5° (MeCN); 3-CF3, Et, H, Ph, 128-40°/0.35, 182-5°; 3,4-Cl2, Et, H, 2-MeOC6H4, 210-20°/0.7, 221-5° (Et2O, EtOH); 4-Cl, Et, H, 2-ClC6H4, 210-20°/0.7, 211-13° (Et2O, EtOH); 3-Cl, Et, H, 2-MeOC6H4, 170-90°/0.7, 213-17° (Et2O, EtOH); 3-Cl, Et, H, Ph, 180-200°/0.7, 191-3° (Et2O, EtOH); 4-F, Et, H, 3-MeC6H4, 160-5°/0.8, 193-6° (Et2O, EtOH); 4-F, Et, 3-Me, Ph, 170-5°/0.6, 228-32° (Et2O, EtOH).

IT 745-59-5P, Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl- 905-90-8P, Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride
RL: PREP (Preparation)
(preparation of)

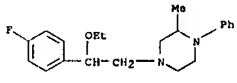
RN 745-59-5 CAPLUS

CN Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



RN 905-90-8 CAPLUS

CN Piperazine, 4-(β-ethoxy-p-fluorophenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



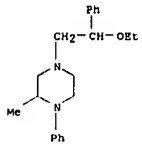
●2 HCl

L9. ANSWER 123 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:15362 CAPLUS
DOCUMENT NUMBER: 62:15362
ORIGINAL REFERENCE NO.: 62:2782f-h
TITLE: Piperazines
PATENT ASSIGNEE(S): CIBA Ltd.

SOURCE: 17 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| NL 6400466 | | 19640724 | NL 1964-466 | 19640122 <-- |
| PRIORITY APPLN. INFO.: | | | US | 19630123 |

GI For diagram(s), see printed CA Issue.
AB I were prepared by refluxing 11.8 g. EtOPhCHCH2Cl and 12.5 g. N-(2-methoxyphenyl)piperazine in 200 ml. BuOH containing 40 g. Na2CO3 24 hrs., the inorg. material filtered, and the filtrate evaporated to give I (R = 2-MeOC6H4, R1 = H), b0.9 179-80°; di-HCl salt m. 215-17° (EtOH-MeCN). The following I were similarly prepared (R, R1, b.p./mm., m.p. hydrochloride, and crystallization solvent given): Ph, H, 177-80°/0.35, 225-8° (di-HCl salt), --; 2-ClC6H4, H, 200-5°/0.55, 200-3°, AcCH2CO2Et; Ph, Me, 165-80°/0.5, 230-5°, EtOH; 3-MeC6H4, H, 185-90°/0.2, 197-9°, EtOH; 2-pyridyl, H, 185-90°/0.5, 125-30°, EtOH-Et2O. I, their N-oxides, and quaternary salts can be used as antiinflammatory or vasodilation agents.
IT 853-92-9
(Derived from data in the 7th Collective Formula Index (1962-1966))
RN 853-92-9 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)

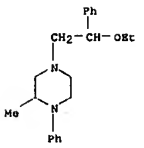


●2 HCl

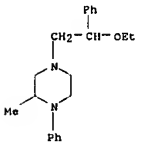
IT 853-91-8P, Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl- 3020-53-9P, Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, hydrochloride
RL: PREP (Preparation)
(preparation of)
RN 853-91-8 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)







RN 3020-53-9 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

L9 ANSWER 124 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:15361 CAPLUS
DOCUMENT NUMBER: 62:15361
ORIGINAL REFERENCE NO.: 62:2782e-f
TITLE: Diisopropylamine orotate
INVENTOR(S): Masusawa, Kuniyasu; Irikura, Tsutomu
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd.
SOURCE: 1 p.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

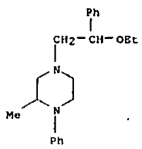
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 39008847 | B4 | 19640528 | JP | 19610304 <-- |
| PRIORITY APPLN. INFO.: | | | JP | 19610304 |

AB A solution of 4 g. orotic acid in 20 cc. H2O is stirred with 2.59 g. diisopropylamine and evaporated in vacuo at below 50° to give 5.7 g. title compound, plates, m. 210-15°, useful as a H2O-soluble orotic acid derivative
IT 853-92-9
(Derived from data in the 7th Collective Formula Index (1962-1966))





RN 853-92-9 CAPLUS
CN Piperazine, 4-(β-ethoxyphenethyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



●2 HCl

L9 ANSWER 125 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:425459 CAPLUS
DOCUMENT NUMBER: 61:25459
ORIGINAL REFERENCE NO.: 61:4373f-h,4374a
TITLE: Quaternary salts of 5-(4-alkylpiperazino)dibenzo[a,d]cycloheptadienes
INVENTOR(S): Rhone-Poulenc, S. A.
SOURCE: 15 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

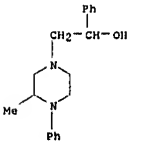
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| BE 633454 | | 19631210 | BE | <-- |
| DE 1197891 | | | DE | |
| FR 1403619 | | | FR | |
| FR CAM61 | | | FR | |
| GB 1041536 | | | GB | |
| NL 294074 | | | NL | |
| US 3257404 | | 19660621 | US 1963-285859 | 19630606 <-- |
| PRIORITY APPLN. INFO.: | | | FR | 19620615 |

GI For diagram(s), see printed CA Issue.
AB 5-(4-Alkylpiperazino)dibenzo[a,d]cycloheptadienes (I) were converted to quaternary salts (II) with Me2SO4. These compds. showed spasmolytic, ganglioplegic, and atropinic activities more pronounced than the corresponding I. 5-Chlorodibenzo[a,d]cycloheptadiene (Mychajlyszyn and Protiva, CA 54, 9766a) (9.14 g.) in 150 cc. anhydrous PhMe was refluxed 4 h. with 8.00 g. 1-methylpiperazine in 30 cc. PhMe, the reaction mixture treated with 120 cc. water, 80 cc. Et2O, and 5 cc. aqueous NaOH (d. 1.33), the water layer washed with 100 cc. Et2O, the combined organic layers extracted 3 times with a total 440 cc. 2N NaOH, the acid exts. washed with 150 cc. Et2O and basified with 50 cc. aqueous NaOH (d. 1.33) and 50 cc. water, the resulting oil extracted 3 times with a total 400 cc. Et2O, and the combined Et2O exts. dried over K2CO3 and evaporated to yield 6.45 g. I (R = Me) (III), m.





111° (iso-PrOH). To 9.9 g. III in 200 cc. anhydrous Me2CO was added dropwise in 10 min. 4.3 g. Me2SO4 in 10 cc. anhydrous Me2CO, the temperature rising to 27°. The mixture was cooled to room temperature in 3 h. to yield 11.9 g. II (R = Me), m. 190-3°, washed twice with a total 70 cc. anhydrous Me2CO. Similarly prepared were the following homologs (R, m.p. of I, and m.p. of II given): Et, 90°, 168-70°; Pr, 84°, 201-3°; Bu, 78°, 207-9°; HOCH2CH2, 129°, 144-6°; PhCH2, 120-1°, 218-22°; iso-Pr, 87°, 201-3°; cinnamyl, 142°, 214-16°; PhCH2CH2, 99-100°, 160-70°; HOCH2CH2OCH2CH2, - (di-HCl salt m. 170°), 150°.
IT 94437-01-1P, 1-Piperazineethanol, 3-methyl-α,4-diphenyl-
RL: PREP (Preparation)
(preparation of)
RN 94437-01-1 CAPLUS
CN 1-Piperazineethanol, 3-methyl-α,4-diphenyl- (7CI) (CA INDEX NAME)



L9 ANSWER 126 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:425458 CAPLUS
DOCUMENT NUMBER: 61:25458
ORIGINAL REFERENCE NO.: 61:4373b-f'
TITLE: 2-(4-Phenylpiperazino)-1-phenylethyl acetates
INVENTOR(S): Shapiro, Seymour L.; Freedman, Louis; Soloway, Harold
PATENT ASSIGNEE(S): U.S. Vitamin & Pharmaceutical Corp.
SOURCE: 4 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

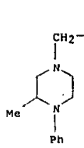
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 3135756 | | 19640602 | US | 19610517 <-- |
| PRIORITY APPLN. INFO.: | | | US | 19610517 |

GI For diagram(s), see printed CA Issue.
AB The title esters are prepared and can be used as bronchodilators. Thus, a solution of 17.8 g. 1-phenylpiperazine in 35 ml. iso-PrOH is added to a mixture of 25 g. p-ClC6H4COCH2Br in 65 ml. iso-PrOH and the mixture refluxed 15 min. to give 63% 1-(p-chlorophenacyl)-4-phenylpiperazine-HBr (I.HBr), m. 242-4° (decomposition) (MeOH), which is treated with NaOH to give I, m. 132-3° (EtOH). A mixture of 11.9 g. I in 100 ml. EtOH is treated with 0.65 g. NaBH4 to give 58% 2-(4-phenylpiperazino)-1-(p-chlorophenyl)ethanol (II), m. 154-5° (EtOH). A mixture of 3.2 g. II,

20 g. Ac2O, and 25 ml. MeCN is refluxed 9 hrs. to give 57% 2-(4-phenylpiperazino)-1-(p-chlorophenyl)ethyl acetate, m. 109-10° (hexane). Similarly prepared are the following III (X = CHOAc)(R, R1, and m.p. or b.p./mm. given): H, H (IV), 113-15°; (X = CHO2CEt) H, H, 132-4°/0.005; (X = CH2O2CPr) H, H, 186-90°/0.05; (X = CHOBz), H, H, [HCl salt m. 130-3° (Me2CO)]; (X = CHO2CNHEt) H, H, 184-5°; (X = CHO2CNHEt) H, H, 126-7° (MeCN); H, p-Cl, 109-10°; H, p-Br, 118-19°; H, 2,4-Me2, 100-1°; o-Me, H, 99-101°; m-Me, H, 109-10°; p-Me, H, 88-9°; o-Cl, H, 90-1°; m-Cl, H, 95-7°; p-Cl, H, 123-4°; o-MeO, H, 200-6°/0.005; p-MeO, H, 87-8°. Also prepared is the analog of IV derived from 1-phenyl-2-methylpiperazine (IVa), m. 68°. Also prepared are the following III (X = CHOH) (R, R1, and m.p. or b.p./mm. given): H, H (V), 113° [HCl salt m. 184-5° (EtOH)]; o-Me, H, 116-17°; m-Me, H, 95-7°; p-Me, H, 118-19°; o-Cl, H, 129-30° m-Cl, H, 97°; p-Cl, H, 113-14°; o-MeO, H, 196-201°/0.01; p-MeO, H, 144°; H, p-Cl, 154-5°; H, p-Br, 160°; H, 2,4-Me2, 139-40°; H, p-Ph, 180° (MeCN). Also prepared is the analog of V derived from IVa, m. 109-10°. Also prepared are the following III (X = CO, R = H) (R1 and m.p. given): p-Br, 139-40° (EtOH) [HBr salt m. 243-6° (decomposition) (MeOH)]; 2,4-Me2, 110-11° (EtOH), p-Ph, 196-8° (MeCN).

IT 94437-01-1P, 1-Piperazineethanol, 3-methyl-α,4-diphenyl-
97018-29-6P, 1-Piperazineethanol, 3-methyl-α,4-diphenyl-, acetate (ester)
RL: PREP (Preparation)
(preparation of)

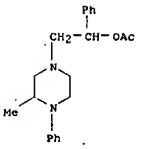
RN 94437-01-1 CAPLUS
CN 1-Piperazineethanol, 3-methyl-α,4-diphenyl- (7CI) (CA INDEX NAME)



RN 97018-29-6 CAPLUS
CN 1-Piperazineethanol, 3-methyl-α,4-diphenyl-, acetate (7CI) (CA INDEX NAME)







L9 ANSWER 127 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:52797 CAPLUS
DOCUMENT NUMBER: 60:52797
ORIGINAL REFERENCE NO.: 60:9296b-d
TITLE: Aminochloro heterocyclic compds.
INVENTOR(S): Weidinger, Hans; Wellenreuther, Gerhard; Bilingsfeld, Heinz
PATENT ASSIGNEE(S): Badische Anilin- & Soda-Fabrik A.-G.
SOURCE: 19 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

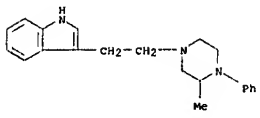
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| FR 1342841 | | 19631115 | FR 1962-909333 | 19620913 <-- |
| DE 1172266 | | | DE | |
| GB 1011984 | | | GB | |
| PRIORITY APPLN. INFO.: | | | DE | 19610913 |

GI For diagram(s), see printed CA Issue.
AB The new compds. were used as intermediates in the manufacture of dyes. A mixture containing 100 parts by weight 2-(4-nitrophenyl)-4-chloroquinazoline suspended in 100 parts by volume Me2CO, 10 parts Raney Ni, and 3 parts by volume Pr3N was hydrogenated at normal pressure at 20-30° to yield 88 parts I (R = H, R1 = p-C6H4NH2). Similarly prepared were 85 parts I (R = H, R1 = m-C6H4NH2) from 100 parts 2-(3-nitrophenyl)-4-chloroquinazoline, and 85 parts I (R = NH2, R1 = Ph) from 100 parts 2-phenyl-4-chloro-6-nitroquinazoline. Also prepared were the following II (R and R1 given): morpholino, m-C6H4-NH2; morpholino, m-C6H4NO2, m. 200-2°; anilino, m-C6H4NH2; anilino, m-C6H4NO2, m. 164-5°; Ph, m-H2NC6H4NH; Ph, m-O2NC6H4NH, 197-9°; morpholino, p-H2NC6H4NH; morpholino, p-O2NC6H4NH, 255-7°.
IT 94961-31-6
(Derived from data in the 7th Collective Formula Index (1962-1966))

RN 94961-31-6 CAPLUS
CN Indole, 3-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (7CI) (CA INDEX NAME)







L9 ANSWER 128 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:52796 CAPLUS
DOCUMENT NUMBER: 60:52796
ORIGINAL REFERENCE NO.: 60:9293g-h,9294a-h,9295a-h,9296a-b
TITLE: Indolylpiperazines
PATENT ASSIGNEE(S): Sterling Drug Inc.
SOURCE: 41 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| GB 944443 | | 19631211 | GB | <-- |
| US 3188313 | | 19650608 | US 1959-842203 | 19590925 <-- |
| PRIORITY APPLN. INFO.: | | | US | 19590925 |

GI For diagram(s), see printed CA Issue.
AB Compds. of type I and II, in which R1 is H, halogen, alkyl, alkoxy, or aryl, R2 is H, alkyl, hydroxyalkyl, or aryl, R3 and R4 is H, alkyl, or aryl, n is 1 to 7, and in which the indole group may be joined in the 2-position or (as shown) the 3-position, were made. These are useful as hypotensive agents, as antinauseants, antipyretics, sedatives, tranquilizers and muscle relaxants; they inhibit apomorphine-induced vomiting, and prolong the narcosis of ether and barbiturates. A solution of 177 g. (PhCH2)2NCH2CH2NHPh, 120 g. ClCH2COCl and 650 ml. CHCl3 was refluxed for 5.5 hrs. to yield 190 g. (PhCH2)2NCH2CH2NPhCOCH2Cl, an oil. This was dissolved in EtOCH2CH2OH, the solution refluxed 4 hrs., cooled, diluted with 650 ml. absolute EtOH, 4 g. Pd-C added, and the mixture reduced by H at 50 lb./in.2 to give 1-phenyl-2-piperazinone (VI), m. 100-5° (p-toluenesulfonate m. 220.2-4.6°). Similarly made from (PhCH2)2NCH2CH2N(4-ClC6H4)(COCH2Cl) (HCl salt m. 161.0-3.8°) was 1-(4-chlorophenyl)-2-piperazinone (HCl salt m. 192.8-4.8°); from 4-benzyl-1-(2,6-dimethylphenyl)-2-piperazinone (HCl salt m. 248.8-54.8°), 1-(2,6-dimethylphenyl)-2-piperazinone (HCl salt m. 224.8-6.0). The I and II were made by various methods. Method A: A mixture of 5.6 g. 2-(3-indolyl)ethyl bromide (VII), 4.1 g. 1-phenylpiperazine, 2.1 g. NaHCO3, and 30 ml. absolute EtOH was refluxed for 6 hrs. to yield 1.4 g. I (R1 = R3 = R4 = H, R2 = Ph, n = 2), m. 131.6-6.0°. Similarly prepared were these I (R3 = R4 = H, n = 2; R1, R2, and m.p. given): H, 4-ClC6H4, 185.2-6.8°; H, p-tolyl, 147.8-54.8°; 5-MeO, p-tolyl, 108.6-11.0°; H, PhCH:CHCH2, 258.2-63.6°. Also made was 1-[2-(3-indolyl)ethyl]-trans-2,5-dimethylpiperazine, m. 189.2-90.4°, and from VI and VII 1-[2-(3-indolyl)ethyl]-4-phenyl-3-piperazinone, m. 163.2-4.4°. Method B: To a cold solution of 79.2 g. 1-(o-tolyl)piperazine in 500 ml. tetrahydrofuran (VIII) was added 31.2 g. (3-indolyl)glyoxalyl chloride (IX), the white precipitate filtered off, the filtrate evaporated, the residual gum taken up in a warm mixture of 700 ml. H2O.





120 ml. AcOEt and 25 ml. AcOH, and the solid collected, to give 41.5 g. III (R1 = R3 = R4 = H, R2 = o-tolyl) (X). Similarly prepared were these III (R3 = R4 = H; R1, R2, and m.p. given): H, Me, --; H, HOCH2CH2, --; H, m-tolyl, --; H, 2-MeOC6H4, --; H, 4-MeOC6H4, 243-5°; H, 3,4-ClMeC6H3, 211-14°; 6-MeO, Ph, 205-9°; 6-MeO, o-tolyl, 247-50°; 6-MeO, m-tolyl, 206-8°; 6-MeO, p-tolyl, 196-8°; 6-MeO, 2-MeOC6H4, 246-8°; 6-MeO, 4-MeOC6H4, 205-10°; 5-PhCH2O, p-tolyl, 148-55°; 5-PhCH2O, PhCH2CH2, 135-40°; 5-MeS, Ph, 188-91°; 5-MeS, p-tolyl, 211-13°; 5,6-(CH2O2), Ph, 267-9°; 5,6-(CH2O2), o-tolyl, 214.6-15.8°; 5,6-(CH2O2), m-tolyl, 212-16°; 5,6-(CH2O2), p-tolyl, 266.4-78.4°; 5,6-(CH2O2), 2-MeOCH2CH2, 205-9°; 5,6-(MeO)2, Ph, 256.8-8.8°; 5,6-(MeO)2, o-tolyl, 211-16°; 5,6-(MeO)2, m-tolyl, 231-8°; 5,6-(MeO)2, p-tolyl, --; 5,6-(MeO)2, 2-MeOC6H4, 218-22°; 5,6-(MeO)2, 3-MeOC6H4, 234.4-6.4°; 5 6-(MeO), 4-MeOC6H4, 228-36°; 5,6-(MeO)2, 4-MeSC6H4, 236.4-8.2°; 5,6-(EtO)2, Ph, 180.0-1.0°; H, 2-pyridyl, 242-3°; 4-MeO, Ph, --; 5-MeO, Ph, 224-7.5°; 7-MeO, Ph, --; 6-Me, Ph, --; 6-EtO, Ph, 165° (decomposition); 6-MeO, 2-ClC6H4, 125.2-8.8°; 6-MeO, 3-ClC6H4, 214-16°; 6-MeO, 3-MeOC6H4, 211-13°; 6-MeO, 2-EtOC6H4, 180-4°; 6-MeO, 2,6-Me2C6H3, 215-18°; 6-MeO, 5,2-Cl(MeO)C6H3, 208-11°; 5,6-(MeO)2, PhCH2, 210.2-11.8°; 5,6-EtO(MeO), Ph, 215-22°; 5,6-(MeO)2, 2-pyridyl, 249.6-53.6°; 5,6-(OCH2CH2O), Ph, 172.5-8.5°; 5,6-(MeO)2, 2-EtOC6H4, 135-43°; 5,6-(MeO)2, 2,6-Me2C6H3, 253.2-6.2°; 5,6-(CH2O2), 4-MeOC6H4, 257-8°; 5,6-(CH2O2), 2-BuOC6H4, 164-7.5°; 5,6-(EtO)2, 2-MeOC6H4, 188-6.5°; 5,6-(EtO)2, 3-MeOC6H4, 162-5.5°; H, Ph, 224.2-5.6°; H, PhCH2, 174.4-5.6°; 5,6-(MeO)2, 2-ClC6H4, .apprx.214°; 6-Cl, Ph, 270-4°; 6-MeO, 2-pyridyl, 231-3°; 5,6-(MEO)2, 2-BuOC6H4, 171-4°; 5,6-(MeO)2, 2-EtC6H4, 193-8°; 5,6-(MeO)2, 2,5-(MeO)2C6H3, 208-10°; 5,6-(CH2O2), 2-pyridyl, 271-3°; 5,6-(MeO)2, 2-MeSC6H4, 219-21°. Also prepared were these III (R1, R2, R3, R4, and m.p. given): H, Ph, Me, H, --; 5,6-(MeO)2, Ph, Me, H, 163-74°; 5,6-(CH2O2), 4-MeOC6H4, Me, H, 173-266°; 5,6-(CH2O2), Ph, H, Me, 219-19.8°; 5,6-(MeO)2, Ph, H, Me, 215-22°; H, Ph, Me, Me, --; 6-MeO, Ph, Me, H, 218-20°; 6-MeO, Ph, Ph, H, 155-60°; 5,6-(MeO)2, 2-MeOC6H4, Me, H, 211.4-12.6°; 5,6-(MeO)2, o-tolyl, Me, H, 119-22°; 5,6-(MeO)2, m-tolyl, Me, H, 120-2°; 5,6-(MeO)2, 3-MeOC6H4, Me, H, 159-63.5°; 5,6-(CH2O2), 2-MeOC6H4, Me, H, 233-5°; 5,6-(MeO)2, Ph, Et, H, 177-84°; 5,6-(EtO)2, Ph, Me, H, 182-7°. A solution of 41.5 g. X in 250 ml. VIII was added to a suspension of 27 g. LiAlH4 in 300 ml. VIII, and the mixture refluxed 61/2 hrs. to give 28.5 g. I (R1, R3, R4 = H, R2 = o-tolyl, n = 2), m. 124.2-6.4°. Similarly prepared were these I (R3 = R4 = H, n = 2; R1, R2, and m.p. given): H, H, 149.8-52.0°; H, Me, -- (di-HCl salt m. 279.0-83.8°); H, HOCH2CH2, -- (di-HCl salt m. 266.8-71.4°); H, m-tolyl, 163.8-6.2°; H, 2-MeOC6H4, 111.4-14.2°; H, 4-MeOC6H4, 129.8-31.6°; H, 3,4-ClMeC6H3, 159.2-60.6°; 6-MeO, Ph, 137.4-9.6°; 6-MeO, o-tolyl, 139.2-41.4°; 6-MeO, m-tolyl, 119.8-23.4°; 6-MeO, p-tolyl, 172.2-3.4°; 6-MeO, 2-MeOC6H4, 98.2-100.2°; 6-MeO, 4-MeOC6H4, 185.6-8.6°; 5-PhCH2O, p-tolyl, 161.4-3.6°; 5-PhCH2O, PhCH2CH2, 121-3°; 5-MeS, Ph, 110.2-11.6°; 5-MeS, p-tolyl, 111-13.6°; 5,6-(CH2O2), Ph, 141.0-3.2°; 5,6-(CH2O2), o-tolyl, 159.2-60.8°; 5,6-(CH2O2), m-tolyl, 130.0-1.4°; 5,6-(CH2O2), p-tolyl, 187.0-8.8°; 5,6-(CH2O2), 2-MeOC6H4, 158.0-9.4°; 5,6-(MeO)2, Ph, 128.4-30.0°; 5,6-(MeO)2,

o-tolyl, -- (HCl salt m. 218.4-23.4°); 5,6-(MeO)2, m-tolyl, 118.4-19.6°; 5,6-(MeO)2, p-tolyl, 137.8-9.2°; 5,6-(MeO)2, 2-MeOC6H4, 116.0-16.6°; 5,6-(MeO)2, 3-MeOC6H4, 123.0-4.0°; 5,6-(MeO)2, 4-MeOC6H4, 158.8-64.0°; 5,6-(MeO)2, 4-MeSC6H4, 175.4-7.2°; 5,6-(EtO)2, Ph, 123.0-5.2°; H, 2-pyridyl, -- (HCl salt m. 232.2-4.4°); 4-MeO, Ph, 177.2-82.2°; 5-MeO, Ph, 147.4-50.0°; 7-MeO, Ph, 122.0-5.2°; 6-Me, Ph, 174.2-5.2°; 6-EtO, Ph, 159.6-63.2°; 6-MeO, 2-ClC6H4, 125.2-8.8°; 6-MeO, 3-ClC6H4, 103.6-4.4°; 6-MeO, 3-MeOC6H4, 142.0-4.6°; 6-MeO, 2-EtOC6H4, 159.4-61.4°; 6-MeO, 2,6-Me2C6H3, 135.2-6.8°; 6-MeO, 2,5-MeOC1C6H3, 121.8-8.6°; 5,6-(MeO)2, PhCH2 (XI), 113-14.4°; 5,6-EtO(MeO), Ph, 129.2-30.6°; 5,6-(MeO)2, 2-pyridyl -- (HCl salt m. 210.2-11.8°; 5,6-(OCH2CH2O), Ph, 170.8-6.8°; 5,6-(MeO)2, 2-EtOC6H4, 120.4-2.0°; 5,6-(MeO)2, 2,6-Me2C6H3, 117.8-19.6°; 5,6-(CH2O2), 4-MeOC6H4, 182.4-4.6°; 5,6-(CH2O2), 2-BuOC6H4, 125.0-6.4°; 5,6-(EtO)2, 2-MeOC6H4, 89.4-92.0°; 5,6-(EtO)2, 3-MeOC6H4, 97.6-8.4°; 6-Cl, Ph, 177.2-8.6°; 6-MeO, 2-pyridyl, 107.2-8.2°; 5,6-(MeO)2, 2-BuOC6H4, 93.8-5.8°; 5,6-(MeO)2, 2-EtC6H4, 104.2-7.2°; 5,6-(MeO)2, 2,5-(MeO)2C6H3, 136.8-7.8°; 5,6-(CH2O2), 2-pyridyl, -- (di-HCl salt m. 200-24°); 5,6-(MeO)2, 2-MeSC6H4, 116-17.8°. Also made were these I (n = 2; R1, R2, R3, R4, and m.p. given): H, Ph, Me, H, 154.2-5.6°; 5,6-(MeO)2, Ph, Me, H, -- (HCl salt m. 249.0-55.4°); 5,6-(CH2O2), 4-MeOC6H4, Me, H, 160.8-2.8°; 6-MeO, Ph, Me, H, -- (HCl salt m. 253.2-6.2°); 6-MeO, Ph, Ph, H, 148.2-8.8°; 5,6-(MeO)2, 2-MeOC6H4, Me, H, -- (di-HCl salt m. 217.4-20.8°); 5,6-(MeO)2, o-tolyl, Me, H, 119.8°-21.6°; 5,6-(MeO)2, m-tolyl, Me, H, -- (di-HCl salt m. 210.2-3.8°); 5,6-(MeO)2, 3-MeOC6H4, Me, H, -- (di-HCl salt m. 182.6-4.2°); 5,6-(CH2O2), 2-MeOC6H4, Me, H, 137.0-43.0°; 5,6-(CH2O2), 2-MeOC6H4, H, Me, 155.4-6.4°; 5,6-(MeO)2, Ph, Me, H, 139.6-40.4°; 5,6-(MeO)2, Ph, Et, H, --(HCl salt m. 237.6-9.0°); 5,6-(EtO)2, Ph, Me, H, 111.6-13.2°; 5,6-(CH2O2), 2-MeOC6H4, Me, Me, 118.2-19.6°; 5,6-(CH2O2), 2-MeOC6H4, Me, PhCH2, 169.2-70.2°; H, 2-MeOC6H4, H, Me, 74.6-6.4°. Catalytic debenzylation of XI gave I (R1 = 5,6-(MeO)2, R2, R3, R4 = H, n = 2), m. 109.6-11.4°, which reacted with 2-chloropyrimidine to give I (R1 = 5,6-(MeO)2, R2 = 2-pyrimidinyl, R3, R4 = H, n = 2), m. 127.2-8.2°. III (R4 = alkyl was reduced to II; other II were obtained as by-products in the LiAlH4 reduction of III. Thus were made these II (n = 1; R1, R2, R3, R4, and m.p. given): 5,6-(CH2O2), Ph, H, Me, 171-2.5°; 5,6-(MeO)2, Ph, H, Me, 128.4-30.2°; H, Ph, Me, Me, 136.8-9.6°; 5,6-(MeO)2, p-tolyl, H, H, 193.2-8.0°. Method C: On addition of 3-(4-benzhydryl-1-piperazinyl)propionyl chloride to a solution of 5-chloroindole and EtMgBr in ether, there was obtained IV (R1 = 5-Cl, R2 = Ph2CH, R3, R4 = H, n = 2) (XII), which with MeI and NaNH2 in liquid NH3 gave IV (R1 = 5-Cl, R2 = Ph2CH, R3 = H, R4 = Me, n = 2). Similarly made were these IV (R1, R2, R3,R4, and n given): H, Ph, Ph, H, 3; H, Ph, Ph, PhCH2, 3. XII was reduced by LiAlH4 to I (R1 = 5-Cl, R2 = Ph2CH, R3, R4 = H, n = 3), but XII reduced by NaBH4 yielded II (R1 = 5-Cl, R2= Ph2CH, R3 = R4 = H, n = 2). When IV (R4 = alkyl) was reduced by LiAlH4, then II was obtained. Thus were made these II (R1, R2, R3, R4 and n given): 5-Cl, Ph2CH, H, Me, 2; H, Ph, Ph, PhCH2, 3; 6-BuO, Me, H, 4-MeSC6H4CH2CH2, 3; 5,6,7-(MeO)3, Me, H, 4-BuOC6H4CH2CH2, 3; H, Me, H, 3-HOC6H4CH2CH2, 3; H, Me, H, PhCH:CHCH2, 3. Method D: To a cold solution of 22.5 g. 3-indoleacetic acid and 13.3 g. Et3N in 800 ml. Me2CO was added 18.1 g. ClCO2Bu-iso, the mixture stirred for 10 min. at -10°, a solution of 1-phenylpiperazine in little Me2CO added,





and the mixture kept 1.7 hrs. at room temperature to yield 5.4 g. V(R1, R2 = H, R3 = Ph, n = 1), m. 179.4-81.6°. Similarly prepared were these V (R3 = H; R1, R2, n, and m.p. given): H, Ph, 2, 136.2-7.4°; H, 3-MeOC6H4, 1, --; H, 2-ClC6H4, 2, --; H, o-tolyl, 2, --; H, 2-MeOC6H4, 2, 173.0-6.0°; H, Ph, 3, --; H, 2-MeOC6H4, 3, 129-32°; H, 3-MeOC6H4, 3, --; 6-MeO, Ph, 2, 169-72°; 6-MeO, 2-MeOC6H4, 2, 120.5-2.0°; 5,6-(MeO)2, 3-ClC6H4, 1, --; 5,6-(CH2O2), Ph, 2, 178-80°; 5,6-(MeO)2, 2-ClC6H4, 1, 185-8.5°; 5,6-(MeO)2, 2-MeOC6H4, 2, 124.8-7.4°; 5,6-(MeO)2, Ph, 2, 120.5-2.0°; 5,6-(MeO)2, 3-MeOC6H4, 2, --. Also obtained was V (R1 = 5,6-(MeO)2, R2 = Ph, R3 = Me, n = 2). Also made was 1-[3-(1-indolyl)propionyl]-4-phenylpiperazine, an oil and 1-[3-(2-methyl-5,6-dimethoxy-3-indolyl)propionyl]-4-phenylpiperazine. By reduction of these V by LiAlH4 in VIII were prepared these I (R3 = R4 = H; R1, R2, n, and m.p. given): H, Ph, 2, --; H, Ph, 3, 126.6-7.8°; H, 3-MeOC6H4, 2, 146.4-7.6°; H, 2-ClC6H4, 3, 140.3-3.6°; H, o-tolyl, 3, 102.4-4.2°; H, 2-MeOC6H4, 3, 156.8-9.2°; H, Ph, 4, 96.0-100.8°; H, 2-MeOC6H4, 4, 120.6-3.8°; H, 3-MeOC6H4, 4, -- (HCl salt, m. 234.2-5.8°); 6-MeO, Ph, 3, 196.4-7.6°; 6-MeO, 2-MeOC6H4, 3, 153.2-5.0°; 5,6-di-MeO, 3-ClC6H4, 2, --(HCl salt m. 236.8-9.2°); 5,6-(CH2O2), Ph, 3, 142.6-4.2°; 5,6-(MeO)2, 2-ClC6H4, 2, 86.8-9.8°; 5,6-(MeO)2, 2-MeOC6H4, 3, 120.4-1.4°; 5,6-(MeO)2, Ph, 3, 157.4-8.2°; 5,6-(MeO)2, 3-MeOC6H4, 3, 159.0-60.2°. Also made was I (R1 = 5,6-(MeO)2, R2= Ph, R3 = Me, R4 = H, n = 3), m. 117.8-18.8°, and 1-[3-(1-indolyl)propyl]-4-phenylpiperazine, m. 96.7-8.4°. Method E: A solution of 9.0 g. indole in 100 ml. dioxane was added to a cold solution of 6.25 ml. 40% aqueous CH2O and 13.3 g. 1-phenylpiperazine in 1 l. dioxane to give I (R1 = R3 = R4 = H, R2 = Ph, n = 1), m. 184.6-6.8°. Similarly made was I (R1 = 5,6-(MeO)2, R2 = Ph, R3 = R4 = H, n = 1), m. 159.3-60.2°. Method F: The piperazine ring was formed after a substituted ethylenediamine group had been joined to the indole moiety. Thus, 27 g. IX and 58 g. (PhCH2)NPhCH2CH2NH2 in 300 ml. VIII refluxed for 5 hrs. gave 41.9 g. N-benzyl-N-phenyl-N'-[(3-indolyl)glyoxalyl]ethylenediamine, m. 162.2-2.8°, which was reduced by LiAlH4 to N-benzyl-N-phenyl-N'-[2-(3-indolyl)ethyl]ethylenediamine (XIII) (di-HCl salt m. 171.4-5.4°). Also made were N-benzyl-N-methyl-N'-[(3-indolyl)glyoxalyl]ethylenediamine, m. 124.5-7.0°, and N-benzyl-N-methyl-N'-[2-(3-indolyl)ethyl]ethylenediamine, m. 102-5°. A solution of 11.1 g. XIII and 3.4 g. ClCH2COCl in CH2Cl2 was refluxed to yield 9.4 g. 4-[2-(3-indolyl)ethyl]-1-phenyl-1-benzyl-1m3-oxopiperazinium chloride, m. 157-9.5°, which was catalytically debenzylated to 1-[2-(3-indolyl)ethyl]-4-phenyl-2-piperazinone, m. 157.2-9.0°. Similarly made was 4-[2-(3-indolyl)ethyl]-1-methyl-1-benzyl-3-oxopiperazinium chloride, m. 229.5-32.5°, and 4-[2-(3-indolyl)ethyl]-2-methyl-1-phenyl-3-piperazinone, m. 186.4-91.8°. The latter, reduced by LiAlH4, gave 1-[2-(3-indolyl)ethyl]-3-methyl-4-phenylpiperazine, m. 116.2-17.6°.

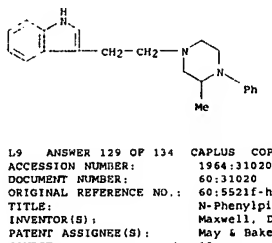
IT 94961-31-6P, Indole, 3-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]-
RL: PREP (Preparation)
(preparation of)

RN 94961-31-6 CAPLUS

CN Indole, 3-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- (7CI) (CA INDEX NAME)







L9 ANSWER 129 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:31020 CAPLUS
DOCUMENT NUMBER: 60:31020
ORIGINAL REFERENCE NO.: 60:5521f-h,5522a-h,5523a
TITLE: N-Phenylpiperazines
INVENTOR(S): Maxwell, Donald R.; Wragg, William R.
PATENT ASSIGNEE(S): May & Baker Ltd.
SOURCE: 12 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| GB 943739 | | 19631204 | GB 1959-9836 | 19590320 <-- |
| PRIORITY APPLN. INFO.: | | | GB | 19590320 |

AB p-O2N C6H4CH2CH2Br (11.5 g.), 16.2 g. N-phenylpiperazine (I), and 150 cc. CHCl3 refluxed 24 hrs. gave Ia (R = p-O2NC6H4CH2CH2, R1 = H), m. 140-1° (CHCl3-EtOH), which was hydrogenated over Pt.2 to give the p-amino analog; di-HCl salt (II) m. 314-17°. Treating the base of II with Ac2O gave the p-acetamido analog, m. 205-8°; isethionate m. 180-2°. Similarly were prepared the following Ia (R, R1, % yield, and m.p. given): p-AcNHC6H4CH2CH2, m-Cl, 57, 174-6°; p-O2NC6H4CH2CH2, o-Cl, 68, 108-10°; p-H2NC6H4CH2CH2, o-Cl, 52, - (di-HCl salt m. 306-9°); p-O2NC6H4CH2CH22, m-Cl, 59, 83-5°; p-H2NC6H4CH2CH2, m-Cl, 57, - (di-HCl salt m. 285-8°); p-O2NC6H4CH2CH2, p-Cl, 58, 147-9°; p-H2NC6H4CH2CH2, p-Cl, 61, - (di-HCl salt m. 319-22°); p-OHCNHC6H4CH2CH2, H, 100, 163-5° (HCl salt m. 255° (decomposition)]; p-OHCNHC6H4CH2CH2, m-Cl (III), 67, 147-50°; p-OHCNMeC6H4CH2CH2, H, 95, 130-1°. An alc. solution of dl-p-MeNC6H4CH2CHMeNH2 (IV) and PhN(CH2CH2Br)2 was refluxed 5.5 hrs., the mixture cooled, treated with Na2CO3, and refluxed 6 hrs. to give 32% dl-Ia (R = p-MeNC6H4CH2CHMe, R1 = H), m. 114-15°. IV.2HCl, m. 213-16°, was obtained by LiAlH4 reduction of p-dimethylamino β-methyl-β-nitrostyrene, m. 120-1°, obtained in 79% yield by condensing p-Me2NC6H4CHO with EtNO2 in C6H6. II and ClCO2Me in CHCl3 gave 77% Ia (R = p-MeO2CNHC6H4CH2CH2, R1 = H), m. 158-9°. Prepared also was 39% Ia (R = p-MeO2CNHC6H4CH2CH2, R1 = o-Cl), m. 124-5°, 98% Ia.HCl (R = p-ClCH2CH2O2CNHC6H4CH2CH2, R1 = H) (V), m. 256° (decomposition) (free base m. 133-5°), and 76% Ia.HCl (R = p-ClCH2CH2O2CNHC6H4CH2CH2, R1 = o-Cl) (VI), m. 233-5°. Addition of Br in glacial HOAc to p-H2NC6H4CH2CH2Br.HCl gave 78% 2-(4-amino-3,5-dibromophenyl)ethyl bromide, m. 96-9°, which was refluxed with I to give 47% 1-[2-(4-amino-3,5-dibromophenyl)ethyl]4-phenylpiperazine, m. 106-7°. Refluxing V with alc. KOH gave 14% 3-[4-[2-(4-phenylpiperazinyl)ethyl]phenyl]oxazolid-2-one, m. 194-6°. Refluxing VI with alc. KOH gave 77% Ia (R = p-HOCH2CH2NHC6H4CH2CH2, R1 =



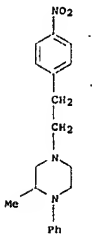


o-Cl), m. 113-14°. Ia (R = p-H2NCONHC6H4CH2CH2, R1 = H), m. 315-18°, was obtained in 42% yield by refluxing an aqueous solution of NaCNO and II. Refluxing p-nitrostyrene bromohydrin and I in toluene gave 57% dl-Ia [R = p-O2NC6H4CH(OH)CH2, R1 = H), m. 167-8°, reduced catalytically to 80% the amino analog, m. 144-5 °. I and p-MeO3BNHC6H4CH2CH2Br, m. 104-5°, from MeO3BCl and p-aminophenethyl bromide, was refluxed to give 63% Ia (R = p-MeO3BNHC6H4CH2CH2, R1 = H), m. 153-5°. III in tetrahydrofuran was added to LiAlH4, and the mixture refluxed to give 83% Ia (R = p-MeNHC6H4CH2CH2, R1 = m-Cl), m. 96-8°. Refluxing I and p-F3CCONHC6H4CH2CH2Br, m. 107-11°, from p-H2NC6H4CH2CH2Br and trifluoroacetic anhydride, gave 40% Ia (R = p-F3CCONHC6H4CH2CH2, R1 = H), m. 170-2°. p-FC5H4NH2 and diethanolamine was treated with HBr, the mixture heated to 180-90°, and H2O distilled to give 30% N-p-fluorophenylpiperazine, b0.1 118-23°, which was converted into Ia (R = p-O2NC6H4CH2CH2, R1 = p-F), m. 127-9°. This, when hydrogenated, gave 57% the amino analog; HCl salt m. 280-4°. Prepared similarly were 47% N-m-fluorophenylpiperazine-HBr, m. 232-5°, 54% Ia (R = p-O2NC6H4CH2CH2, R1 = m-F), m. 118-20°, and 62% the p-H2N analog as HCl salt, m. 282-5°. Ethylene oxide was treated with m-anisidine to give N,N-bis(β-hydroxyethyl)m-anisidine, which was treated with POCl3 to give 74% N,N-bis(β-chloroethyl)-m-anisidine as an oil. This when added to a mixture of p-nitrophenethylamine-HCl and anhydrous Na2CO3 in BuOH and refluxed gave 54% Ia (R = p-O2NC6H4CH2CH2, R1 = m-MeO), m. 118-20°, which was hydrogenated to give 67% the p-amino analog as HCl salt, m. 255-8°. Similarly prepared were 77% N,N-bis(β-hydroxyethyl)-o-fluoroaniline, b4 141-7°, 95% N,N-bis(β-chloroethyl)-o-fluoroaniline, 62% Ia (R = p-O2NC6H4CH2CH2, R1 = o-F), m. 118-20°, Ia. HCl (R = p-H2NC6H4CH2CH2, R1 = o-F), m. 239-41°, 48% N-m-bromophenylpiperazine-HBr, m. 215-18°, 65% Ia (R = p-O2NC6H4CH2CH2, R1 = m-Br), m. 238-41°, Ia.2HCl (R = p-H2NC6H4CH2CH2, R1 = m-Br), m. 256-9°, 69% Ia (R = p-O2NC6H4CH2CH2R1 = o-Me), m. 103-3°, 73% Ia.2HCl(R = p-H2NC6H4CH2CH2, R1 = o-Me), m. 315-17°, 57% Ia (R = p-O2NC6H4CH2CH2, R1 m-Me), m. 115-17°, 66% Ia.2HCl (R = p-H2NC6H4CH2CH2, R1 = m-Me), m. 303-5°, 30% N-(2-methyl-5-chlorophenyl)piperazine-HBr, m. 265-7°, 36% Ia (R = p-O2NC6H4CH2CH2, R1 = 2,5-MeCl), m. 87-8°, 60% Ia.2HCl (R = p-H2NC6H4CH2CH2, R1 = 2,5-MeCl), m. 325-7°, 52% N-(3,5-dichlorophenyl)piperazine-HBr, m. 309-13°, 58% Ia [R = p-O2NC6H4CH2CH2, R1 = 3,5-Cl2), m. 92-4°, 56% Ia (R =p-H2NC6H4CH2CH2, R1 = 3,5-Cl2), m. 91-2°, 42% N,N-bis(β-hydroxyethyl)-2,3-dichloroaniline, b0.08 170-82°deg, 52% Ia (R = p-O2NC6H4CH2CH2, R1 = 2,3-Cl2), m. 145-7°, 55% Ia.HCl (R = p-H2NC6H4CH4CH2, R1 = 2,3-Cl2), m. 241-3°, 21% N-(3,4-dichlorophenyl)piperazine, b15 202°, 67% Ia (R = p-O2NC6H4CH2CH2, R1 = 3,4-Cl2), m. 119-20°, 57% Ia.3HCl (R = p-H2NC6H4CH2CH2, R1 = 3,4-Cl2), m. 326-8°, 47% dl-1-[2-(p-nitrophenyl)ethyl]-3-methyl-4-phenylpiperazine, m. 108°, 39% dl-1-[2-(p-aminophenyl)ethyl]-3-methyl-4-phenylpiperazine-HCl, m. 265-9°, 34% Ia (R = p-O2NC6H4CH2CH:CHCH2, R1 = H), m. 117-18°, 28% Ia. HCl [R = p-H2NC6H4(CH2)4, R1 = H], m. 275-8°, 4-(2-chloro-4-nitrophenyl)but-2-enyl chloride, m. 47-8°, Ia (R = 2,4-Cl(O2N)C6H3CH2CH:CHCH2, R1 = H], m. 94-5°, 35% 2-(4-methoxy-3-nitrophenyl)ethyl bromide, m. 52-3°, 68% Ia [R = 3,4-(O2N)(MeO)C6H3CH2CH2, R1 = H), m. 106-7°, 65% Ia [R = 3,4-(H2N)(MeO)C6H3CH2CH2, R1 = H), m. 147-8°, 61% Ia.HCl (R = p-H2NC6H4CH2CH:CHCH2, R1 = H), m. 246-7°, Ia. HCl [R = 2,4-Cl(H2N)C6H3CH2CH:CHCH2, R1 = H], m. 228-31°, 54% 4-chloro-p-acetamidobutyrophenone, m. 162-4°,

13% Ia (R = p-AcNHC6H4CO(CH2)3, R1 = H), m. 172-4°, 63% 4-(m-nitro-p-fluorophenyl)-4-oxobutyl chloride, m. 63-4°, Ia [R = 4,3-F(O2N)C6H3CO(CH2)3, R1 = H], m. 110-12°, 16% Ia [R = 4,3-F(H2N)C6H3CO(CH2)3, R1 = H], m. 147-50°, 76%, dl-N(β-hydroxyethyl)-N-(β-hydroxypropyl)aniline, b0.15 135-42° 26%, dl-1-[2-(p-nitrophenyl)ethyl]-2-methyl-4-phenylpiperazine', m. 82-4°, and 75% dl-1-[2-(p-aminophenyl)ethyl]-2-methyl- 4-phenylpiperazine-HCl, m. 247-50°. These compds. had pharmacological and psychotropic properties.

IT 94915-72-7P, Piperazine, 2-methyl-4-(p-nitrophenethyl)-1-phenyl- 100175-11-9P, Piperazine, 4-(p-aminophenethyl)-2-methyl-1-phenyl-, hydrochloride
RL: PREP (Preparation)
(preparation of)

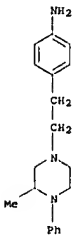
RN 94915-72-7 CAPLUS
CN Piperazine, 2-methyl-4-(p-nitrophenethyl)-1-phenyl- (7CI) (CA INDEX NAME)



RN 100175-11-9 CAPLUS
CN Piperazine, 4-(p-aminophenethyl)-2-methyl-1-phenyl-, hydrochloride (7CI) (CA INDEX NAME)







●x HCl

L9 ANSWER 130 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:9840 CAPLUS
DOCUMENT NUMBER: 60:9840
ORIGINAL REFERENCE NO.: 60:1774f-h
TITLE: Piperazines
INVENTOR(S): Stevens, George de; Mull, Robert P.
PATENT ASSIGNEE(S): CIBA Ltd.
SOURCE: 31 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| BE 615259 | | 19620919 | BE | <-- |
| FR 1332560 | | | FR | |
| GB 995036 | | | GB | |
| PRIORITY APPLN. INFO.: | | | US | 19610320 |

GI For diagram(s), see printed CA Issue.

AB The title compds. (I) and their salts are valuable pharmaceuticals, especially vasodilators and diagnostic agents of low toxicity. They have adrenolytic properties. 2-Methyl-1-phenylpiperazine (8.8 g.) was dissolved in 50 cc. PhMe, 2.4 g. 53% suspension of NaH in mineral oil added, the mixture refluxed 2 hrs., 11.6 g. 5-ethoxy-3-(4-methylphenyl)propyl chloride added, the mixture refluxed overnight and filtered, and the filtrate evaporated in vacuo and distilled to give I (Ar = 4-MeC6H4, R = Et, R1 = Me, X = Ph), b0.2 182-4°; di-HCl salt m. 190-2° (EtOH). Similarly, the following I were prepared (Ar, R, R1, X, b.p./mm., and m.p. of di-HCl salt given): Ph, Et, Me, Ph, 168-70°/0.075, 194°; 4-ClC6H4, Et, Me, Ph, 210-15°/0.27, 174-6°; 4-ClC6H4, Me, Me, Ph, 170°/0.05, 184°; 4-MeC6H4, iso-Pr, Me, Ph, 146-54°/0.04 169°; Ph, Et, H, Ph, 160°/0.15, 202-3° (EtOH-Et2O); 4-ClC6H4, Me, H, Ph, 178-80°/0.1,212-

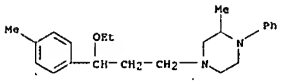




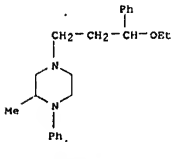
13°; 4-ClC6H4, Et, H, Ph, 168°/0.1, 208°; 4-MeC6H4, Et, H, 2-pyridyl, 162-3°/0.25, - (triHCl salt m. 194-5°).

IT 442-26-2P, Piperazine, 4-(3-ethoxy-3-p-tolylpropyl)-2-methyl-1-phenyl- 745-60-8P, Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl- 748-03-8P, Piperazine, 4-(3-isopropoxy-3-p-tolylpropyl)-2-methyl-1-phenyl- 905-92-0P, Piperazine, 4-[3-(p-chlorophenyl)-3-methoxypropyl]-2-methyl-1-phenyl- 907-68-6P, Piperazine, 4-(3-ethoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride 978-11-0P, Piperazine, 4-[3-(p-chlorophenyl)-3-methoxypropyl]-2-methyl-1-phenyl-, dihydrochloride 1051-75-8P, Piperazine, 4-[3-(p-chlorophenyl)-3-ethoxypropyl]-2-methyl-1-phenyl- 1051-76-9P, Piperazine, 4-[3-(p-chlorophenyl)-3-ethoxypropyl]-2-methyl-1-phenyl-, dihydrochloride 1168-17-8P, Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl-, dihydrochloride 3792-38-9P, Piperazine, 4-(3-isopropoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride
RL: PREP (Preparation)
(preparation of)

RN 442-26-2 CAPLUS
CN Piperazine, 4-[3-ethoxy-3-(4-methylphenyl)propyl]-2-methyl-1-phenyl- (9CI) (CA INDEX NAME)



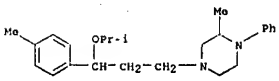
RN 745-60-8 CAPLUS
CN Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



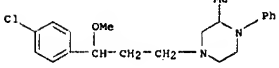
RN 748-03-8 CAPLUS
CN Piperazine, 4-(3-isopropoxy-3-p-tolylpropyl)-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)



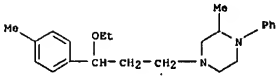




RN 905-92-0 CAPLUS
CN Piperazine, 4-[3-(p-chlorophenyl)-3-methoxypropyl]-2-methyl-1-phenyl- (8CI) (CA INDEX NAME)

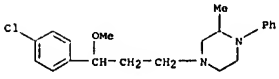


RN 907-68-6 CAPLUS
CN Piperazine, 4-(3-ethoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



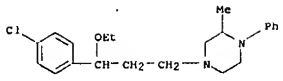
●2 HCl

RN 978-11-0 CAPLUS
CN Piperazine, 4-[3-(p-chlorophenyl)-3-methoxypropyl]-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)

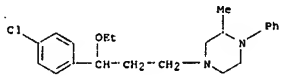


●2 HCl

RN 1051-75-8 CAPLUS
CN Piperazine, 4-[3-(p-chlorophenyl)-3-ethoxypropyl]-2-methyl-1-phenyl- (7CI, 8CI) (CA INDEX NAME)

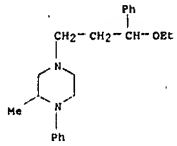


RN 1051-76-9 CAPLUS
CN Piperazine, 4-[3-(p-chlorophenyl)-3-ethoxypropyl]-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)



●2 HCl

RN 1168-17-8 CAPLUS
CN Piperazine, 4-(3-ethoxy-3-phenylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)

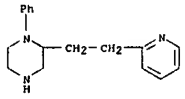


●2 HCl

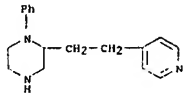
RN 3792-38-9 CAPLUS
CN Piperazine, 4-(3-isopropoxy-3-p-tolylpropyl)-2-methyl-1-phenyl-, dihydrochloride (7CI, 8CI) (CA INDEX NAME)







RN 97018-75-2 CAPLUS
CN Piperazine, 1-phenyl-2-[2-(4-pyridyl)ethyl]- (7CI) (CA INDEX NAME)



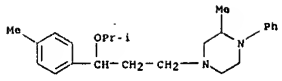
L9 ANSWER 132 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1963:6735 CAPLUS
DOCUMENT NUMBER: 58:6735
ORIGINAL REFERENCE NO.: 58:1086c-e
TITLE: Two-component diazotype layers
PATENT ASSIGNEE(S): Kalle A.-G.
SOURCE: 9 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| BE 611215 | | 19620606 | BE | <-- |
| DE 1226878 | | | DE | |
| GB 955886 | | | GB | |
| US 3139341 | | 19640630 | US 1961-156117 | 19611130 <-- |
| PRIORITY APPLN. INFO.: | | | DE | 19601209 |

AB The preparation of a two-component diazotype material containing in the light-sensitive layer a piperazine derivative of the general structure I, where R and R' are lower alkyl groups and R'' is an alkyl, aralkyl, aryl, CO2H, or carbalkoxy group, and a diazonium salt is described. A solution of MeOCH2CH2OH 45, MeCOEt 45, H2O 10 parts, citric acid 1.5, B(OH)3 1.6 parts, sulfosalicylic acid 0.6 parts, 3,5-dimethyl-2-(4-methyl-1-piperazinylmethyl)phenol, m. 99-100°, 4.5 and [3,4-Me(EtNH)C6H3N2]BF4 4.0 parts coated onto a cellulose acetate film, and the dried film exposed under a transparency to the light of a 12-amp. arc and developed in the usual manner with NH3 vapor gave a yellow transparency of the original suitable for further reproduction.
IT 99750-96-6, Mesitol, α4-(3-methyl-4-phenyl-1-piperazinyl)-, hydrochloride
(in diazotype process)
RN 99750-96-6 CAPLUS
CN Mesitol, α4-(3-methyl-4-phenyl-1-piperazinyl)-, hydrochloride (7CI)







●2 HCl

L9 ANSWER 131 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1963:462412 CAPLUS
DOCUMENT NUMBER: 59:62412
ORIGINAL REFERENCE NO.: 59:11521a-c
TITLE: N-Aryl-N'-(2-pyridylethyl)piperazines
INVENTOR(S): Boissier, Jacques R.; Ratouis, Roger
PATENT ASSIGNEE(S): Societe Industrielle pour la Fabrication des Antibiotiques (S.I.F.A.)
SOURCE: 11 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

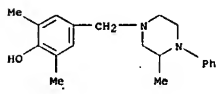
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| FR M1769 | | 19630506 | FR | <-- |
| PRIORITY APPLN. INFO.: | | | GB | 19610317 |
| OTHER SOURCE(S): | | MARPAT 59:62412 | | |

AB N-Arylpiperazines are treated with vinylpyridines in the presence of hydroquinone or tert-butyl-pyrocatechol (I) to give the title compds. which can be used in the treatment of hypertension. Thus, a mixture of 10.5 g. 2-vinyl-pyridine, 18 g. N-phenylpiperazine, and 10 mg. I is heated at 150° for 2 hrs., cooled, the unreacted starting materials distilled under 0.05-0.2 mm. at a bath temperature of 180-200°, and the residue re-crystallized in 400 ml. petr. ether to give 14 g. N-[2-(2-pyridyl)-ethyl]-N'-phenylpiperazine, m. 58°, 53% yield. Similarly prepared are (m.p. given): N-[2-(4-pyridyl)ethyl]-N'-phenyl-piperazine, 83° (petr. ether); N-[2-(2-pyridyl)ethyl]-N'-(2-pyridyl)piperazine, 69° (heptane); N-[2-(4-pyridyl)ethyl]-N-(2-pyridyl)piperazine, 82° (60% aqueous EtOH); N-[2-(2-pyridyl) ethyl]-N'-(2-chlorophenyl)piperazine, 64° (heptane), N-[2-pyridyl)ethyl]-N'-(2-chlorophenyl)piperazine, 69° (hexane); N-[2-(2-pyridyl)ethyl]-N'-(2-methoxyphenyl)piperazine, 47° (hexane); N-[2-(4-pyridyl)ethyl]-N'-(2-methoxyphenyl)-piperazine, 98° (heptane); N-[2-(4-pyridyl)ethyl]-N'-(2-bromo- phenyl)piperazine, 73° (hexane); N-[2-(4-pyridyl)ethyl]-N'-(2-ethoxyphenyl)piperazine, 66° (heptane); and N-[2-(4-pyridyl)-ethyl]-N'-(2-methylphenyl)piperazine, 68°.
IT 97018-74-1P, Piperazine, 1-phenyl-2-[2-(2-pyridyl)ethyl]-
97018-75-2P, Piperazine, 1-phenyl-2-[2-(4-pyridyl)ethyl]-
RL: PREP (Preparation)
(preparation of)
RN 97018-74-1 CAPLUS
CN Piperazine, 1-phenyl-2-[2-(2-pyridyl)ethyl]- (7CI) (CA INDEX NAME)





(CA INDEX NAME)



●x HCl

L9 ANSWER 133 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1961:28013 CAPLUS
DOCUMENT NUMBER: 55:28013
ORIGINAL REFERENCE NO.: 55:5549c-i,5550a-i,5551a-g
TITLE: 1-Arylalkyl-4-arylpiperazines
INVENTOR(S): Janssen, Paul A. J.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| BE 589092 | | 19600415 | BE | <-- |
| DE 1185615 | | | DE | |
| GB 872352 | | | GB | |

AB 1-(γ-Benzoylpropyl)-4-phenylpiperazine, m. 89-90° (6:5 iso-PrOH-H2O), was prepared by reaction of 7.5 g. chlorobutyrophenone and 13.4 g. 1-phenylpiperazine 6 hrs. at room temperature and 4 hrs. at 105-10°; after cooling, 200 g. Et2O was added, the solution dried and evaporated, the residue dissolved in hot 4:1 70% EtOH-Et2O, and precipitated on cooling. The following 1-(arylalkyl)piperazines (1-arylalkyl = γ-benzoylpropyl) were thus prepd (4-aryl group and m.p. given): 3-fluorophenyl, 80.2-1.6° (iso-Pr2O); 3-chlorophenyl, 88-90°; 4-chlorophenyl, 127-8° (10:1 petr. ether-EtOH); 2-tolyl (HCl salt), 205-7° (5:4:3 iso-PrOH-MeOH-acetone); 3-tolyl, 78-9° (13:1 petr. ether-EtOH); 4-tolyl, 87.5-8.5° (iso-PrOH-H2O); 2,5-xylyl (HCl salt), 229-30°; 2-anisyl (di-HCl salt), 207.5-9.5° (iso-PrOH); 4-anisyl, 85-6° (iso-Pr2O); 2-pyridyl, 63-4.8°; 6-methyl-2-pyridyl, 72-5.8°; 4-methyl-2-pyridyl, 65.5-6.5°; 3-cyano-2-pyridyl, 45.5-7°; 5-methyl-2-pyridyl, 71.5-3°; 2-pyrimidyl, 78-9°; 4-methyl-2-pyrimidyl, 62.4-3.2°; 4,6-dimethyl-2-pyrimidyl, 97.4-8°. The following 1-(δ-benzoylbutyl)piperazines: Ph (di-HCl salt), 209-12° (8:8:1 acetone-iso-PrOH-MeOH); 3-tolyl (di-HCl salt), 191.5-2.5°; 2-pyridyl (di-HCl salt), 206.5-7.5°. 1-[γ-(4-Fluorobenzoyl)propyl]piperazines: Ph, 104-6° (iso-PrOH); 3-fluorophenyl (di-HCl salt), 198-200°; 4-fluorophenyl (di-HCl salt), 199.5-201.1°; 4-fluorophenyl (HCl salt), 180.2-1.6° (acetone-iso-PrOH); 3-chlorophenyl (HCl salt), 211-14° (iso-PrOH); 3-chlorophenyl (HCl salt), 197.8-9.5° (acetone-MeOH); 4-chlorophenyl, 96-8° (40:3 petr. ether-EtOH); 2-tolyl (HCl salt), 238-41° (decomposition); 3-tolyl (di-HCl salt),

210-13° (decomposition); 4-tolyl, 99-101° (iso-PrOH-H2O); 2,5-xylyl (di-HCl salt), 237.5-9.5°; 2-anisyl, 67.5-8.5° (iso-Pr2O) (di-HCl salt m. 205-5.5°); 4-anisyl, 104.6-5.5° (iso-PrOH), 5-methyl-2-pyridyl, 92-3°; 4-methyl-2-pyrimidyl (di-HCl salt), 215-20°. 1-[γ-(4-Chlorobenzoyl)propyl]piperazines: Ph, 113.5-14.5°; 3-chlorophenyl, 86-8°; 3-tolyl, 99.6-110.4°; 4-tolyl, 129.5-30.5°; 4-anisyl, 126.6-7.8°; 4-fluorophenyl (HCl salt), 207-9°; 4-chlorophenyl, 127-8.5°; 2-pyridyl, 82.5-4.4°. 1-[γ-(4-Methylbenzoyl)propyl]piperazines: Ph, 103-4.8°; 2-chlorophenyl, 106-7°, 3-chlorophenyl, 124.5-5.5°; 4-chlorophenyl, 134.5-6°; 3-tolyl, 87-8.5°; 4-tolyl, m. 117.2-19.2°; 2-pyridyl, 92-3°; 4-anisyl, 123.2-4°. 1-[γ-(2,5-Dimethylbenzoyl)propyl]piperazines: Ph (HCl salt), 179.5-80.5°. 1-[γ-(4-Anisoyl)propyl]piperazines: 3-fluorophenyl, m. 111-13°; 2-chlorophenyl, 73.5-3.8°; 3-iodophenyl, -; 3-chlorophenyl, 101.6-2.4°; 4-chlorophenyl, 128.6-30°; 2-tolyl (HCl salt), 239.5-40.5°; 3-tolyl, 105-6°; 4-tolyl, 126.6-7.6°; 2,5-xylyl (HCl salt), 225-6°; 2-anisyl (di-HCl salt), 197-8.2°; 4-anisyl, 125.6-7.4°. 1-[γ-(2,4-Dimethoxybenzoyl)propyl]piperazines: Ph (di-HCl salt), 195-6°; 2-tolyl (HCl salt), 177-9.2°; 2-anisyl (HCl salt), 214-15°; 2-pyridyl, 84.5-5.5°; 4-methyl-2-pyridyl, 79-80.8°. 1-[γ-(3,4-Dimethoxybenzoyl)propyl]piperazines: Ph, 101-3.5°; 2-pyridyl, 104.5-6.9°; 4-methyl-2-pyridyl, 85.4-6.5°. 1-[γ-(2,5-Dimethoxybenzoyl)propyl]piperazines: Ph(di-HCl salt), 179-80°. 1-[γ-(2,3,4-Trimethoxybenzoyl)propyl]piperazines: Ph, 113-16.2°. 1-[γ-(4-Ethoxybenzoyl)propyl]piperazines: Ph, 125.2-6.8°; 3-tolyl, 113.4-13.8°. 1-(β-Methyl-γ-benzoylpropyl)piperazines: Ph (di-HCl salt), 219.5-21.5°; 3-tolyl, 82.8-3.8° (petr. ether); 2-anisyl (di-HCl salt), 193-7°. 1-[γ-(4-Iodobenzoyl)propyl]piperazines: 5-methyl-2-pyridyl, -; 2-pyridyl, -; 4-methyl-2-pyrimidyl (di-HCl salt), -; 2-thiazolyl, -. 1-[γ-(4-Methoxybenzoyl)propyl]piperazines: 6-methyl-2-pyridyl, 74.6°; 4-methyl-2-pyridyl, 69.5-70.5°; 5-methyl-2-pyridyl, 84.6-6°; 3-cyano-2-pyridyl, 73.5-5.5°; 2-pyrimidyl, 83-3.5°; 2-thiazolyl (di-HCl salt), 122-4°; 4-methyl-2-pyrimidyl, 90°; 4,6-dimethyl-2-pyrimidyl, 71.8-4.2°; 2-(4-methyl)thiazolyl, 62.5-72° (di-HCl salt m. 187-201°); 2-(5-methyl-1,3,4-thiadiazolyl), 111.5-12.5°. 1-[γ-(2-Thenoyl)propyl]piperazines: 2-pyridyl, 70-1°; 5-methyl-2-pyridyl, 89.5-90.5°; 4-methyl-2-pyridyl, 65-6°; 6-methyl-2-pyridyl, 107.5-8.5°; 3-cyano-2-pyridyl, 71.5-2.5°; 2-pyrimidyl, 57.5-8.6°; 4-methyl-2-pyrimidyl, 52-3° (di-HCl salt m. 214.8-17°); 4,6-dimethyl-2-pyrimidyl, 64.5-5.6°; 2-thiazolyl, 52.2-4.6°; 2-(4-methyl)thiazolyl (di-HCl salt), 163-6°; 2-(5-methyl-1,3,4-thiadiazolyl), 83.6-5.6°, Ph (HCl salt), 186-7°; 3-fluorophenyl, 68.2-70.2°; 2-chlorophenyl (HCl salt), 202.5-3°; 3-chlorophenyl, 103.6-4.6°, 4-chlorophenyl, 94.5-6.5°; 2-tolyl (HCl salt), 212-13°; 3-tolyl, 74-5°; 4-tolyl, 77.5-8.5°; 2,5-xylyl (di-HCl salt), 214-15°; 2-anisyl (di-HCl salt), 197-201.8°; 4-anisyl, 69-70°. 1-[γ-(4-Fluorobenzoyl)propyl]piperazines: 4,6-dimethyl-2-pyrimidyl, 85.5-7.5°; 2-pyrimidyl, 111.6-12.8°; 2-thiazolyl, 74.5-6.5°; 2-(5-methylthiazolyl), 73-5.2°, 2-(5-methyl-1,3,4-thiadiazolyl), 105-6°, 2-(1,3,4-thiadiazolyl), 94.6-5.8°. 1-(γ-Benzoylpropyl)piperazines: 2-thiazolyl,





61.5-4°; 2-(4-methylthiazolyl)(di-HCl salt), 186-8°; 2-(1,3,4-thiadiazolyl), 59-64°; 2-(5-methyl-1,3,4-thiadiazolyl), 98-100.2°. 1-(γ-Benzoylpropyl)-4-(4-fluorophenyl)piperazine di-HCl salt, m. 214.5-17° (1:2:2 acetone-iso-PrOH-MeOH), was prepared by heating in a sealed tube 72 hrs. at 145-50° 9.1 g. γ-chlorobutyrophenone, 23 g. 1-(4-fluorophenyl)piperazine, and 0.1 g. KI, extracting the cooled mixture with H2O and Et2O, and treating the dried organic layer with dry HCl; the base was liberated in aqueous alkaline solution, m. 104-5.5° (EtOH). 1-[γ-(4-Anisoyl)propyl]-4-phenylpiperazine, m. 126.6-7.5°, and the corresponding 4-fluorophenyl derivative, m. 121.2-1.8°, 1-[γ-(2-thenoyl)propyl]-4-phenylpiperazine-2HCl, decomposed at 203-5°, and the 4-fluorophenyl analog, m. 82.5-3°, were similarly prepared 1-[γ-(4-Fluorobenzoyl)propyl]-4-(3-methyl-2-pyridyl)piperazine-HCl, m. 212-20° (iso-Pr2O), was prepared from 4.4 g. γ-chloro-4-fluorobutyrophenone and 7.8 g. 1-(3-methyl-2-pyridyl)piperazine in 120 cc. C6H6 in a sealed tube at 125° 24 hrs. The following derivs. were similarly prepared 1-[γ-(4-Fluorobenzoyl)propyl] compound (4-aryl and m.p. given): 4-methyl-2-pyridyl, 79.5-81°; 3-cyano-2-pyridyl, 71.5-3.5°; 6-chloro-3-pyridazinyl, 152-3.9°. 1-[γ-(4-Methoxybenzoyl)propyl] compound: 6-chloro-3-pyridazinyl, 176-6.8°. 1-[γ-(2-Thenoyl)propyl] compound: 6-chloro-3-pyridazinyl, 138-8.8°; 6-methoxy-3-pyridazinyl, 98.8-9.8°. 1-(γ-Benzoylpropyl)-4-benzoylpiperazine, m. 85-6° (iso-Pr2O), was prepared by heating a stirred mixture of 7 g. 1-(γ-benzoylpropyl)piperazine, 60 g. C6H6, 50 g. 10% NaOH solution, and (dropwise) 4.5 g. BzCl, and keeping the mixture at 70° 45-60 min. The following 1-(γ-benzoylpropyl) compds. were similarly prepared (same data): 4-fluorobenzoyl (HCl salt), 214.5-16.5°; 2-chlorobenzoyl (HCl salt), 216-17.5°; 3-chlorobenzoyl (HCl salt), 210.5-12.5°; 4-chlorobenzoyl, 98-9°; 3-trifluoromethylbenzoyl, 77.5-9°; 2-anisoyl (HCl salt), 140.8-3°; 2,6-dimethoxybenzoyl (oxalate); 193.1-4.8°; 3,4,5-trimethoxybenzoyl (oxalate), 187.4-8.2°; 5-(3-methyl-1,2,4-thiadiazolyl), 78-9°; 3-carboxamido-2-pyridyl, 112.6-14.2°. 1-[γ-(4-Fluorobenzoyl)propyl] compds.: benzoyl (HCl salt), 228-32.5°. 1-[γ-(4-Anisoyl)propyl] compds.: benzoyl (HCl salt), 200.2-3.2°; 4-fluorobenzoyl, 65.2-6.2°; 2-anisoyl, 97-8.2°; 2,6-dimethoxybenzoyl (oxalate), 201.5-1.8°. 1-[γ-(2-Thenoyl)propyl] compds.: 4-fluorobenzoyl, 82.5-3.5°; 4-nicotinoyl, 64.6-5.8°; 2-thenoyl, 85.6-7.4°. 1-Phenyl-4-(4-phenylpiperazinyl)-1-butanol-2-HCl, m. 198-200°, was prepared by reaction of 8.5 g. 1-(γ-benzoylpropyl)-4-phenylpiperazine and 0.25 g. NaBH4 in 160 cc. absolute EtOH 2 hrs. at 45° and decomposition with 2N HCl; the distillation residue was treated with aqueous alkali solution, extracted with Et2O, and treated with dry HCl. Following 1-phenyl-4-(R-substituted-piperazinyl)-1-butanols were similarly prepared (R given); 4-(3-tolyl), 83.5-4.5°; 4-(4-tolyl), 90.2-1.8°; 4-(3-fluorophenyl), 70-1.5°; 4-(3-chlorophenyl), 99-9.9°; 4-(4-chlorophenyl), 105-6°; 4-(4-anisyl), 91.5-2.6°; 4-(4-methyl-2-pyrimidyl), 78.5-80°; 4-(2-pyridyl), 113.8-14.8°. 1-(4-Tolyl) analogs: 4-Ph, 104-5.6°; 4-(4-tolyl), 105-6°; 4-(4-anisyl), 84-5°; 4-(2-pyridyl), 119.2-19.8°. 1-(2,5-Xylyl) analogs: 4-Ph, 92.8-3.8°. 1-(4-Fluorophenyl) analogs: 4-Ph, 85.5-7.5° (HCl salt m. 143.5-6.5°); 4-(3-chlorophenyl), 100-1.8°; 4-(4-chlorophenyl), 112.5-13.8°; 4-(2-anisyl), 105-6°; 4-(4-tolyl), 93-5°; 4-(2-pyridyl), 104-5°. (4-Chlorophenyl)





analogs: 4-Ph, 93.5-5°; 4-(3-chlorophenyl), 84-5°; 4-(4-chlorophenyl), 132-3°; 4-(3-tolyl), 93-4.5°. 1-(4-Anisyl) analogs: 4-Ph, 104.2-7.2°; 4-(2-chlorophenyl), 106.8-8.4°; 4-(3-tolyl), 119.5-21.5°; 4-(4-tolyl), 109.5-10.2°. 1-(4-Ethoxyphenyl) analogs: 4-Ph, 113-14.8°. 1-(2-Thienyl) analogs: 4-Ph, 91.4-3°; 4-(3-tolyl), 76-8°; 4-(4-tolyl), 113-14°; 4-(3-fluorophenyl), 78-9°; 4-(4-chlorophenyl), 109.2-10°; 4-(2-chlorophenyl), 85.5-7.5°; 4-(3-chlorophenyl), 81.5°; 4-(2-pyridyl), 95-7°; 4-(2-pyrimidyl), 97.6-9.4°. 1-Phenyl-5-(4-phenylpiperazinyl)-1-pentanol, m. 111-12°, and 1-phenyl-5-[4-(3-tolyl)piperazinyl]-1-pentanol, m. 107.4-9.2°, were also prepared 1-[γ-(4-Anisoyl)propyl]-4-(6-methyl-2-pyridyl)piperazine, m. 74-6°, was prepared by heating 8 hrs. at 110° 6.2 g. γ-chloro-4-methoxybutyrophenone and 8.9 g. 1-(6-methyl-2-pyridyl)piperazine. 1-(γ-Benzoylpropyl)-4-(6-methylthio-3-pyridazinyl)piperazine, m. 124-5°, was prepared by heating in a sealed tube 48 hrs. at 140-50°, 14.8 g. 1-(γ-benzoylpropyl)piperazine, 5 g. 3-chloro-6-(methylthio)pyridazine, 120 g. toluene, and 0.01 g. KI. N-(4-Tolylsulfonyl)-N-(β-hydroxyethyl)-N-(β-hydroxypropyl)amine (I), m. 66.2-8.2° (iso-PrOH and petr. ether at -20°), was prepared by adding 190.5 g. 4-toluenesulfonyl chloride to 119 g. N-(β-hydroxyethyl)-N-(β-hydroxypropyl)amine and 54 g. Na2CO3 in 450 g. H2O at 70°, heating 1 hr. at 95°, cooling, and extracting with Et2O. Reaction of 450 g. I and 690 g. SOCl2 at 125° 1 hr., yielded N-(4-tolylsulfonyl)-N-(β-chloroethyl)-N-(β-chloropropyl)amine (II). Adding slowly 9.3 g. aniline in 15 cc. cyclohexanol to a hot mixture of 31 g. II, 32 g. Na2CO3, 0.1 g. KI, and 215 g. cyclohexanol, refluxing 48 hrs., cooling, filtering, adding C6H6, Et2O, H2O, and concentrated HCl precipitated 1-(4-tolylsulfonyl)-3-methyl-4-phenylpiperazine-HCl (III), m. 214-20° (decomposition). Powdered 3-methyl-4-phenylpiperazine-2HBr, m. 193.4-9° (decomposition), was prepared by stirring at 30° 24 hrs. 93.5 g. III, 71.7 g. phenol, and 570 g. 30% HBr in AcOH, treating the product with Et2O, then boiling acetone. The free base in 4-methyl-2-pentanone was refluxed 22 hrs. with 11.2 g. γ-chloro-4-fluorobutyrophenone, 12.7 g. Na2CO3, and 0.1 g. KI; the product was treated with active C, then with dry HCl in Et2O to yield 1-[γ-(4-fluorobenzoyl)propyl]-3-methyl-4-phenylpiperazine-2HCl, m. 227-34.5° (decomposition). Following 1-substituted-3-methyl-4-substituted-piperazines were similarly prepared (1- and 4-substituents and m.p. given); γ-benzoylpropyl, Ph (di-HCl salt), 229-33° [4-(2-anisyl) analog (di-HCl salt) m. 212-15°]; γ-(4-anisoyl)propyl, Ph, 92-3.8° [4-(2-anisyl) analog (di-HCl salt) m. 199-200°]; γ-(2-thenoyl)propyl, Ph (di-HCl salt), 214-15.5° [4-(2-anisyl) analog (di-HCl salt) m. 213-14.5°]; γ-(4-fluorobenzoyl)propyl,, 2-anisyl (di-HCl salt), 212-13°. 1-[γ-(4-Anisoyl)propyl]-4-phenylpiperazine, m. 85-6.2°, was obtained by adding dropwise 180.9 g. 1-phenyl-4-(cyanopropyl)piperazine in 700 cc. Et2O to a stirred solution of 211 g. 4-anisylmagnesium bromide in 700 cc. Et2O, refluxing 1 hr., treating with dilute HCl, heating gently the aqueous solution 1 hr., and extracting the alkalized solution with CHCl3.

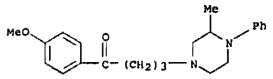
IT 2946-76-1P, Piperazine, 2-methyl-1-phenyl- 102758-21-4P, Butyrophenone, 4'-methoxy-4-(3-methyl-4-phenyl-1-piperazinyl)- 108983-89-7P, 1-Butanone, 4-(3-methyl-4-phenyl-1-piperazinyl)-1-(2-thienyl)-, dihydrochloride 110531-91-4P, Butyrophenone, 4-(3-methyl-4-phenyl-1-piperazinyl)-, dihydrochloride
RL: PREP (Preparation)
(preparation of)





RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 102758-21-4 CAPLUS
CN Butyrophenone, 4'-methoxy-4-(3-methyl-4-phenyl-1-piperazinyl)- (6CI) (CA INDEX NAME)



RN 108983-89-7 CAPLUS
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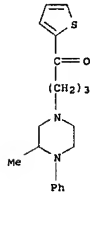
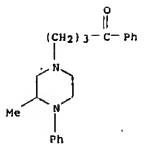


●2 HCl

RN 110531-91-4 CAPLUS
CN Butyrophenone, 4-(3-methyl-4-phenyl-1-piperazinyl)-, dihydrochloride (6CI) (CA INDEX NAME)



●2 HCl

L9 ANSWER 134 OF 134 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1955:36037 CAPLUS
DOCUMENT NUMBER: 49:36037
ORIGINAL REFERENCE NO.: 49:6967e-i,6968a-b
TITLE: Derivatives of piperazine. XXIV. Synthesis of 1-arylpiperazines and amino alcohol derivatives
AUTHOR(S): Pollard, C. B.; Wicker, Thomas H., Jr.
CORPORATE SOURCE: Univ. of Florida, Gainesville
SOURCE: Journal of the American Chemical Society (1954), 76, 1853-5
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB cf. C.A. 48, 7616a. A series of 8 1-arylpiperazines (I) have been prepared by the reaction of mixed HCl salts of aromatic amines and diethanolamines. Derivs. of the I were prepared by the reaction with ethylene oxide (II), 3-methoxypropylene oxide (III), Ac2O, BzCl, and PhNCS. p-ClC6H4NH2 (280.6 g.) and 210.3 g. (HOCH2CH2)2NH carefully neutralized with 375 cc. 37% HCl (d. 1.19), the mixture heated with continuous removal of the H2O, neutralized with 180 g. NaOH in 300 cc. H2O, and the resulting oily layer distilled gave 205 g. (52.3%) 1-(4-chlorophenyl)piperazine (IV), b5 155.7-7.2°, m. 71.5-3.5°. Similarly were prepared the following I [1-aryl and other substituents if present, % yield, b.p./mm., d20, and nD25 given]: p-MeC6H4 (V), 25.5, 150.9-2.5°/10, -, -; m-MeC6H4 (VI), 22.8, 154.2-6.2°/10, 1.0383, 1.5744; o-MeC6H4 (VII), 26.5, 136.5-7.5°/10, 1.0261, 1.5600; m-ClC6H4 (VIII), 38.4, 157.2-8.2°/5, 1.1897, 1.5985; o-ClC6H4 (IX), 32.7, 133.9-4.9°/5, 1.1763, 1.5794; 1-Ph, 2-Me (X), 30.7, 138.5-40.5°/10, 1.0410, 1.5723; 1-Ph, 3-Et (XI), 20.3, 147.8-9.8°/10, 1.0327, 1.5635. IV shaken with a slight excess of BzCl in the presence of excess 10% aqueous NaOH and the product recrystd. from EtOH gave the 4-Bz derivative of IV, m. 128.0-9.5°. Similarly were prepared the 4-Bz derivs. (m.p. given) of: V.HCl, 201.6-3.6°; VI.HCl, 202.6-4.6° (decomposition); VII, 122.5-3.5° VIII.HCl, 158.3-9.8°; IX, 130.5-32°. IV refluxed 0.5 hr. with a 4-fold excess of Ac2O, the mixture poured into 100 cc. ice water, neutralized with solid Na2CO3, and the product recrystd. from EtOH gave the 4-Ac derivative of IV, m. 99.5-101.5°. Similarly were prepared the 4-Ac derivs. (m.p. given) of: V, 109.5-10.5° (from H2O); VI, 46.7-8.2°; VII, 55.9-7.9° VIII, 42.2-4.2°; IX, 65.5-6°; X, 57.4-9.4°; all derivs. (except that of V) separated



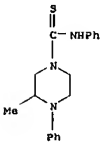


as oils and were dissolved in Et2O, dried with K2CO3, and the residue from the Et2O solution recrystd. from heptane. IV (19.66 g.) in 100 cc. MeOH treated during 15 min. with 8.8 g. III, the mixture refluxed 3 hrs., the MeOH removed in vacuo, the residue cooled, and the resulting solid recrystd. from heptane yielded 13.5 g. (47.5%) 1-(4-chlorophenyl)-4-(2-hydroxy-3-methoxypropyl)piperazine, m. 78-9.5°. Similarly were prepared the 4-(2-hydroxy-3-methoxypropyl) derivs. (% yield and m.p. given) of: V, 61, 77.5-79°; VI, 44.6, 56.5-7.5°; VII, 46.7, 38-9°; VIII, 34.4, 58.8-9.8°; IX, 70.4, 90-1.5°; X, 56, -, b0.3 151.5-3.5°. II (4.405 g.) introduced near the bottom of a solution of 19.66 g. IV in 100 cc. MeOH at such a rate as to avoid boiling, the mixture stirred several hrs. at room temperature, the MeOH evaporated on the steam bath, and the residue cooled and recrystd. from heptane gave 19.5 g. (81.2%) 1-(4-chlorophernyl).4-(2-hydroxyethyl)piperazine, m. 107-8.5°. Similarly were prepared the 4-(2-hydroxycthyl) derivs. (% yield and m.p. or b.p./mm. given) of: V, 35.5, 51.5-2.5°; VI, 31.8, 67-8.5°; VII, 65.6, 146-9°/1.5 (di-HCl salt, m. 175.1-6.6°); VIII, 33, 97.5-8.6°; IX, 55, 166-9°/2.3 (mono-HCl salt, m. 154.2-5.7°); X, 74, 167-72°/1 (di-HCl salt, m. 235.2-6.5°); XI, 67, 156-8.2°/2.2.

IT 2946-76-1P, Piperazine, 2-methyl-1-phenyl- 4318-46-1P, 1-Piperazinecarboxanilide, 3-methyl-4-phenylthio- 856839-29-7P, Piperazine, 4-acetyl-2-methyl-1-phenyl-
RL: PREP (Preparation)
(preparation of)

RN 2946-76-1 CAPLUS
CN Piperazine, 2-methyl-1-phenyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

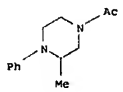
RN 4318-46-1 CAPLUS
CN 1-Piperazinecarboxanilide, 3-methyl-4-phenylthio- (7CI, 8CI) (CA INDEX NAME)



RN 856839-29-7 CAPLUS
CN Piperazine, 4-acetyl-2-methyl-1-phenyl- (5CI) (CA INDEX NAME)







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L3 STRUCTURE UPLOADED
L4 4 S L3 FULL

FILE 'CAPLUS' ENTERED AT 16:01:46 ON 18 SEP 2007
L5 1 S L4 FULL

FILE 'REGISTRY' ENTERED AT 16:07:59 ON 18 SEP 2007
L6 STRUCTURE UPLOADED
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FILE 'CAPLUS' ENTERED AT 16:08:40 ON 18 SEP 2007
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L9 134 S L8 AND PY<2003